Fiscal Year 2006 (FY06)
Department of Defense (DOD)
Gulf War Veterans' Illnesses Research Program (GWVIRP)
US Army Medical Research and Materiel Command (USAMRMC)
Broad Agency Announcement (BAA) 06-1 Supplement

All guidelines contained in this FY06 Supplement supersede USAMRMC BAA 06-1 Instructions.

X. Attachments

I. GENERAL INFORMATION

A. Program Name: Department of Defense (DOD) Gulf War Veterans' Illnesses Research Program (GWVIRP).

B. Funding Opportunity Number: W81XWH-06-GWVIRP; a Supplement to the USAMRMC BAA 06-1.

C. Agency Name: USAMRMC, Office of the Congressionally Directed Medical Research Programs (CDMRP), 1077 Patchel Street, Fort Detrick, Maryland 21702-5024.

D. Agency Contact(s)

1. Questions Related to the FY06 GWVIRP Supplement, Proposal Format, or Required Documentation: Principal Investigators (PIs) and Authorized Organizational Representatives (AORs) should submit questions as early as possible. Every effort will be made to answer questions within 5 working days.

Phone: 301-619-7079
Fax: 301-619-7792
Email: cdmrp.pa@amedd.army.mil

2. Questions Related to Pre-application (Pre-proposal and Letter of Intent) Submissions: A help line for questions relating to the electronic submission of pre-proposals and letters of intent is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern time at 301-682-5507. Help also is available on the CDMRP website or by email as follows:

Website: https://cdmrp.org
Email: help@cdmrp.org

3. Questions Related to Electronic Submission of an Invited Full Proposal (through the Grants.gov portal): Issues in submitting applications through the Grants.gov portal should be directed to the Grants.gov help desk at 1-800-518-4726 or email support@grants.gov. The Contact Center hours of operation are Monday through Friday, 7 a.m. to 9 p.m. Eastern time.

E. Anticipated Instrument Type(s): The USAMRMC implements its extramural research program predominantly through the award of grants and cooperative agreements. More information on these funding instruments may be obtained by request from:

Fax: 301-619-2937
Email: qa.baa@amedd.army.mil

F. Catalog of Federal Domestic Assistance (CFDA) Number 12.420: Military Medical Research and Development.

G. Timeline

Proposal submission is a two-step process consisting of (1) pre-application submission and (2) for those invited, full proposal submission. For ***Exploration – Hypothesis Development Awards***, PIs must submit a ***LOI*** and be ***invited*** to submit a full proposal. For ***Investigator-Initiated Research Awards***, PIs must submit a ***pre-proposal*** and be ***invited*** to submit a full proposal.

- **Pre-application Submission Deadline: December 1, 2006**
- **Invitation to Submit Full Proposal: By December 22, 2006**
- **Full Proposal Submission Deadline: February 2, 2007**
- **Peer Review: March 2007**
- **Programmatic Review: April 2007**

II. FUNDING OPPORTUNITY DESCRIPTION

A. Program History: The FY06 GWVIRP was assigned to the USAMRMC CDMRP by Congress with a $5 million dollar budget. The intent of the Program is to fund research focused on chronic illnesses affecting veterans of the 1991 Gulf War.

B. Program Objectives: The primary objective of the GWVIRP is to identify beneficial treatments for veterans affected by Gulf War Illnesses (GWI), either directly by evaluating specific treatments or indirectly by identifying pathophysiological mechanisms underlying these conditions that may subsequently be targeted to developing treatments.

C. Program Priority Areas: The highest priority research projects relate to identification of effective treatment interventions or potential treatment targets for GWI. The two key priority areas for the FY06 GWVIRP include:

1. Identification and evaluation of currently available treatments: The purpose of projects in this category is to identify potentially useful therapeutic interventions for GWI by providing systematic information on currently available treatments in order to identify those that show promise and are suitable candidates for large, randomized clinical trials. Funded projects may include observational studies, experimental studies, or a combination of methods. Possible methods may include retrospective and/or prospective outcomes evaluation, pilot trials, or other innovative designs for providing systematic information on treatment outcomes. Interventions to be evaluated may include conventional medical treatments or complementary therapies. However, a clear rationale must be provided for studies of treatments for which no preliminary evidence exists regarding their utility in treating GWI, GWI-related symptoms, or similar multisymptom conditions such as chronic fatigue syndrome and fibromyalgia.

2. Identification of objective indicators of pathology that distinguish ill from healthy veterans: The focus of projects in this category will be identification of objective measures that distinguish veterans with GWI, or subsets of veterans with GWI, from healthy comparison groups. Highest priority projects will identify measures that can be useful as biomarkers for GWI and shed light on pathophysiological mechanisms potentially amenable to treatment. Animal studies that characterize chronic effects of neurotoxic exposures at dosages comparable to those encountered during the Gulf War may also be funded, if they have direct application to measures of pathophysiology in GWI and are coordinated with studies of ill Gulf War veterans.

D. Award Mechanisms: The FY06 GWVIRP is offering two award mechanisms: (1) the Exploration – Hypothesis Development Award and (2) the Investigator-Initiated Research Award.

1. Exploration – Hypothesis Development Award

a. Intent: The intent of this award is to fund initial exploration of innovative, untested, potentially groundbreaking concepts aimed at identification of beneficial treatment interventions or potential treatment targets for GWI. Results of studies conducted through an Exploration – Hypothesis Development Award may provide the scientific rationale on which a new hypothesis can be based or it may provide initial proof of principle of an innovative hypothesis. The award is designed to provide investigators with the opportunity to pursue serendipitous observations. Some gaps in supporting rationale may exist due to lack of available information. The award is not intended to support ongoing work; the existence of preliminary data suggests that the research proposal should not be submitted to this award mechanism.

b. Key Features

i. Requires submission of a Letter of Intent (LOI) (see Section IV for details).

ii. Projects must address one or both of the FY06 GWVIRP priority areas described in Section II-C.

iii. Projects involving human subjects or specimens will not be supported unless they are exempt under 32 CFR 219.101(b)[1] or qualify for expedited review under 32 CFR 219.110 or 21 CFR 56.110[2]. Studies that do not qualify for exempt status or expedited review will be administratively withdrawn and will not be funded. Proof of exemption or qualification for expedited review is required at the time of full proposal submission (see Attachment 3).

iv. Successfully completed Exploration – Hypothesis Development Awards are expected to lead to high-risk, potentially high-gain research endeavors that will garner

[1] Title 32, Code of Federal Regulations, Part 219, Section 101(b).
[2] For additional information, refer to the U.S. Department of Health and Human Services' Office of Human Research Protections website at http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98

future funding through the CDMRP as available or other funding agencies. Innovation and novelty of concept are important aspects of this award mechanism. It is the responsibility of the PI to clearly and explicitly articulate how the proposed research is innovative and how the concept is novel.

2. Investigator-Initiated Research Award

a. Intent: The intent of this award is to encourage basic or clinical research aimed at identification of beneficial treatment interventions or potential treatment targets for GWI.

b. Key Features

i. Requires submission of a pre-proposal (see Section IV for full details).

ii. Projects must address one or both of the FY06 GWVIRP priority areas described in Section II-C.

iii. Animal, human anatomical and biological substances, human data, and human use studies require submission of a summary that confirms the study's potential for Institutional Animal Care and Use Committee (IACUC) and/or Institutional Review Board (IRB) approval (see Attachments 2 and 3).

iv. Successfully completed Investigator-Initiated Research Awards are expected to significantly advance current concepts and/or methods that drive the target field of knowledge.

E. Award Funding: Budget requests are an important component of the peer and programmatic review evaluation processes. Each award mechanism has specific budget guidelines regarding funding levels for direct costs and the maximum performance period, as noted in the table below. Indirect costs should be added as appropriate. ***Failure to adhere to the budget guidelines below may result in proposal rejection.***

Award Mechanism	Funding Levels (Direct Costs)	Performance Period (Maximum)	Number of Anticipated Awards
Exploration – Hypothesis Development	$25,000 to $75,000	1 year	7
Investigator-Initiated Research	$25,000 to $600,000	4 years	20

Federal Agency Financial Requirements: Proposals from Federal agencies ***must*** provide a plan delineating how all funds will be obligated by September 30, 2007, and how funds will be available to cover research costs over the entire award period. The plan must include the funding mechanism(s) that will be used to carry over funds between fiscal years, such as administrative agreements with foundations, non-Federal institutions, and universities (attach as a PDF to Block 11 of the SF 424 (R&R) Application for Federal Assistance Form discussed in Section V.)

III. ELIGIBILITY INFORMATION

A. Investigators: Investigators at all academic levels (or equivalent) are eligible to submit proposals.

All individuals, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by, or affiliated with, an eligible institution as defined in Section III-B below.

To protect the public interest, the Federal Government ensures the integrity of Federal programs by conducting business only with responsible recipients. The USAMRMC uses the Excluded Parties List System (EPLS) to exclude recipients ineligible to receive Federal awards. The EPLS is online at http://epls.arnet.gov. (Reference Department of Defense Grant and Agreement Regulations [DODGAR] 25.110.)

B. Institutions: Eligible institutions include for-profit, nonprofit, public, and private organizations, such as universities, colleges, hospitals, laboratories, and companies. The USAMRMC is especially interested in receiving applications from Historically Black Colleges and Universities and Minority Institutions (HBCU/MI). Proposals are assigned HBCU/MI status when the submitting institution is so designated by the Department of Education on the date the FY06 GWVIRP Supplement is released. The most current Department of Education list is posted on the CDMRP website at http://cdmrp.army.mil/spp under "Minority Institutions."

Local, state, and Federal Government agencies are eligible to the extent that proposals do not overlap with their fully funded intramural programs. Federal agencies are expected to explain how their proposals do not overlap with their intramural programs.

IV. PRE-APPLICATION SUBMISSIONS AND GUIDELINES

A. Exploration – Hypothesis Development Award Mechanism: Investigators submitting under the Exploration – Hypothesis Development Award Mechanism **MUST submit a Letter of Intent (LOI) and be INVITED to submit a full proposal.**

B. Investigator - Initiated Research Award Mechanism: Investigators submitting under the Investigator - Initiated Research Award Mechanism **MUST submit a Pre-proposal and be INVITED to submit a full proposal.**

C. Letters of Intent and Pre-proposal Submission Deadline: LOIs and pre-proposals *must be submitted electronically* through the CDMRP eReceipt system at https://cdmrp.org by ***5 p.m. Eastern time, December 1, 2006. DO NOT submit a full proposal to the FY06 GWVIRP unless you receive a letter of invitation.***

D. LOI and Pre-proposal Screening: LOIs and pre-proposals will be screened by the GWVIRP Integration Panel (IP) in order to identify proposals aligned with GWVIRP priorities. Invitations to submit a full proposal to the FY06 GWVIRP will be sent to those PIs whose pre-

proposals are selected for further consideration (no later than December 22, 2006). ***DO NOT submit a full proposal to the FY06 GWVIRP unless you receive a letter of invitation*.**

E. LOI Components and Submission: This subsection provides a summary of LOI submission requirements (an LOI is required for Exploration – Hypothesis Development Award pre-application submission).

1. Title/Referral Page: The title/referral page for the LOI will be generated from the information uploaded in CDMRP eReceipt system and appended to the LOI electronically by the eReceipt system.

2. Proposal Information: PIs must submit the Proposal Information as described in the CDMRP eReceipt system at https://cdmrp.org before uploading the LOI.

3. Proposal Contacts: Enter contact information for the PI.

4. Collaborators and Conflicts of Interest (COI): To avoid COI during the screening and review processes, list the names of all scientific participants in the proposed research project including collaborators, consultants, and subawardees.

5. LOI Narrative: The LOI narrative has a ***one-page limit*** inclusive of figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the LOI. The LOI should address the research focus, objectives, specific aims, and anticipated outcomes of the proposed research.

6. Formatting Guidelines and Submission: The LOI should be a PDF file, in accordance with the formatting guidelines specified for full proposal preparation, and uploaded under the "Required Files" tab of the CDMRP eReceipt system.

7. PI's Responsibility: The PI is responsible for uploading the LOI narrative, inclusive of figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the pre-proposal (one-page limit) as a PDF file under the "Required Files" tab of the CDMRP eReceipt system.

8. Authorized Organizational Representative Approval: The Exploration – Hypothesis Development Award LOI does not require approval by the AOR before submission.

9. Administrative Compliance Issues: Compliance guidelines have been designed to ensure the presentation of all LOIs in an organized and easy-to-read manner. The LOI ***will*** be administratively rejected prior to screening if at the LOI submission deadline:

- LOI narrative exceeds page limit.
- LOI narrative is missing.
- The PI does not meet eligibility criteria (as described in Section III).

- Inclusion of GWVIRP IP members in any capacity in the pre-application process. A list of the FY06 GWVIRP IP members may be found at http://cdmrp.army.mil/prmrp/default

The electronic PDF file uploaded in the CDMRP eReceipt system is the official LOI submission file. After conversion of word processing documents to PDF files and before electronic submission, PIs should review their files to ensure that the LOI complies with the formatting guidelines specified for full proposal preparation.

Material submitted after the LOI submission deadline, unless specifically requested by the Government, will not be forwarded for screening.

10. LOI Screening Criteria

a. Impact: How the proposed research will address one or both of the FY06 GWVIRP priority areas.

b. Anticipated Outcomes: How the proposed research is likely to expand the field of knowledge relevant to the targeted priority area(s).

11. LOI Screening: LOIs will be screened by the GWVIRP IP, composed of scientists and clinicians (including representatives from the DOD and the Department of Veterans Affairs [VA]) and a 1991 Gulf War veteran diagnosed with a GWI. PIs who submit LOIs that convey research aligned with the intent of the FY06 GWVIRP Program objectives and priority areas and the funding mechanism selected by the PI will be invited to submit full proposals.

12. LOI Submission Date and Time: LOIs must be received on the CDMRP eReceipt system by ***5:00 p.m. Eastern time, December 1, 2006***.

F. Pre-proposal Components and Submission: This subsection provides a summary of pre-proposal submission requirements (a pre-proposal is required for Investigator-Initiated Research Award pre-application submission).

1. Title/Referral Page: The title/referral page for the pre-proposal will be generated from the information uploaded in CDMRP eReceipt system and appended to the pre-proposal electronically by the eReceipt system.

2. Proposal Information: PIs must submit the Proposal Information as described in CDMRP eReceipt system at https://cdmrp.org before uploading the pre-proposal and supporting documentation.

3. Proposal Contacts: Enter contact information for the PI.

4. Collaborators and Conflicts of Interest (COI): To avoid COI during the screening and review processes, list the names of all scientific participants in the proposed research project including collaborators, consultants, and subawardees.

5. Pre-proposal Narrative: The pre-proposal narrative has a ***five-page limit*** inclusive of figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the pre-proposal. The narrative should address the GWVIRP Program objectives and priority areas, key features of the award mechanism, and the pre-proposal review criteria. Internet URLs directing reviewers to websites containing significant additional information about the proposed research are not allowed in the pre-proposal or its components. Inclusion of such URLs may be perceived as an attempt to gain an unfair competitive advantage. Links to publications referenced in the pre-proposal are allowed.

6. PI's Responsibility: The PI is responsible for uploading the pre-proposal narrative, inclusive of figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the pre-proposal (five-page limit) as a PDF file under the "Required Files" tab of the CDMRP eReceipt system.

7. Formatting Guidelines and Submission: The pre-proposal should be a PDF file, in accordance with the formatting guidelines specified for full proposal preparation, and uploaded under the "Required Files" tab of the CDMRP eReceipt system.

8. Pre-proposal Supporting Documentation: Submit only material specifically requested or required in this FY06 GWVIRP Supplement. *This section is not intended for additional figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, or other information needed to judge the pre-proposal.* Submitting material that was not requested may be construed as an attempt to gain a competitive advantage and such material will be removed; submitting such material may be grounds for administrative rejection of the pre-proposal.

Supporting documentation must be uploaded as a single PDF file under the "Required Files" tab of the CDMRP eReceipt system. The items to be included as supporting documentation are:

a. References: Start section on a new page; one-page limit. List all relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

b. Biographical Sketches: Four-page limit per individual. Include biographical sketches for all key personnel including collaborating investigators and support staff. These documents are a critical component of the review process. Incomplete or missing biographical sketches may result in a lower pre-proposal ranking. A biographical sketch template is provided as Attachment 1.

c. Letters of Collaboration: Include letter(s) of collaboration in cases where the research will be a collaborative effort between two or more institutions.

9. Authorized Organizational Representative Approval: The Investigator-Initiated Research Award pre-proposal does not require approval by the AOR before submission.

10. Administrative Compliance Issues: Compliance guidelines have been designed to ensure the presentation of all pre-proposals in an organized and easy-to-follow manner. Reviewers expect to see a consistent, prescribed format for each pre-proposal. ***Failure to adhere to format requirements makes pre-proposals difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in pre-proposal rejection.*** The entire pre-proposal ***will*** be administratively rejected prior to screening if at the pre-proposal submission deadline:

- Pre-proposal narrative exceeds page limit.
- Pre-proposal narrative is missing.
- The PI does not meet eligibility criteria (as described in Section III).
- Letter of collaboration is missing (in cases involving collaborations between two or more institutions).
- Pre-proposal is incomplete after the deadline.
- GWVIRP IP members are included in any capacity in the pre-application process, including all supporting documentation. A list of the FY06 GWVIRP IP members may be found at http://cdmrp.army.mil/prmrp/default

The electronic PDF file uploaded in the CDMRP eReceipt system is the official pre-proposal submission file. After conversion of word processing documents to PDF files and before electronic submission, PIs should review their files to ensure that the pre-proposal complies with the formatting guidelines specified for full proposal preparation.

For any other sections of a pre-proposal (including supporting documentation) with a defined page limit, any pages exceeding the specified limit will be removed from the pre-proposal and not forwarded for screening. Material submitted after the pre-proposal submission deadline, unless specifically requested by the Government, will not be forwarded for screening.

11. Pre-proposal Screening Criteria

a. Research Strategy and Objectives: Feasibility of successful implementation of the proposed experimental design, rationale, methods, and analyses.

b. Impact: How the proposed research will address one or both of the FY06 GWVIRP priority areas.

c. PI and Key Personnel: How the PI and key personnel are fit to conduct the proposed research.

d. Facilities: The appropriateness of the scientific environment for the proposed research.

e. Projected Budget: How the budget is appropriate for the proposed research.

12. Pre-proposal Screening: Pre-proposals will be screened by the GWVIRP IP, composed of scientists and clinicians (including representatives from the DOD and the Department of Veterans Affairs) and a 1991 Gulf War veteran diagnosed with a GWI. PIs who submit pre-proposals that convey research aligned with the intent of the FY06 GWVIRP Program objectives and priority areas and the award mechanism selected by the PI will be invited to submit full proposals.

13. Pre-proposal Submission Date and Time: Pre-proposals must be received on the CDMRP eReceipt system by ***5:00 p.m. Eastern time, December 1, 2006.***

V. INVITED FULL PROPOSAL COMPONENTS SUMMARY

Invited full proposals must be submitted electronically by the Authorized Organizational Representative through Grants.gov (www.grants.gov) by February 2, 2007. No paper copies will be accepted.

A. Full Proposal Components Summary: ***Do not submit a full proposal*** to the FY06 GWVIRP Exploration – Hypothesis Development Award mechanism or the Investigator-Initiated Research Award mechanism ***unless you have received an invitation to submit a full proposal***. Any full proposal submitted to the FY06 GWVIRP will be rejected if you have not received a full proposal invitation.

This subsection is a summary of the full proposal submission requirements. Details, URLs, and other links are provided in the appropriate subsections of this document. Proposals will be evaluated according to the peer and programmatic review criteria in Section VIII.

Form	Attachment	Action
SF 424 (R&R) Application for Federal Assistance Form		Enter the appropriate information in data fields
Research & Related Other Project Information (R&R OPI) Form	Technical and Public Abstracts (1-page limit each) and Statement of Work (2-page limit)	Attach to Block 6
	Project Narrative (5-page maximum for Exploration – Hypothesis Development Awards; 20-page maximum for Investigator-Initiated Research Awards)	Attach to Block 7
	References Cited and Acronyms and Symbol Definitions	Attach to Block 8
	Facilities & Other Resources	Attach to Block 9
	Description of Existing Equipment	Attach to Block 10
	Publications and/or Patent Abstracts (5-document limit)	Attach to Block 11
	Letters of Institutional Support	Attach to Block 11
	Letters of Collaboration (if applicable)	Attach to Block 11
	Human Biological Substances and Human Subjects Research Review	Attach to Block 11
	Animal Research Review	Attach to Block 11
	Federal Agency Financial Plan (if applicable)	Attach to Block 11
Research & Related Senior/Key Person Profile (Expanded) Form	PI Current/Pending Support	Attach to PI Current & Pending Support field
	PI's Biographical Sketch	Attach to PI Biographical Sketch field
	Key Personnel's Biographical Sketches (4-page limit each)	Attach to Biographical Sketch field for each senior/key person
	Key Personnel's Current/Pending Support	Attach to Current & Pending Support field for each senior/key person
Research & Related Budget Form	Budget Justification	Attach to Section K for each budget period
Research & Related Project/Performance Site Location(s) Form		Enter the appropriate information in data fields
R&R Subaward Budget Attachment(s) (if applicable)		Enter the appropriate information in data fields

During award negotiations, the Certificate of Environmental Compliance, Principal Investigator Safety Program Assurance, and regulatory documents related to human use and animal use will be requested from the PI. At that time, the negotiated indirect rate agreement, Certifications and Assurances for Assistance Agreements, and Representations for Assistance Agreements will be requested from the AOR.

VI. INVITED FULL PROPOSAL INSTRUCTIONS

Each FY06 GWVIRP submission must include the completed package of forms identified in www.grants.gov for the FY06 GWVIRP Supplement. The package includes:

- SF 424 (R&R) Application for Federal Assistance Form,
- Research & Related Other Project Information Form,
- Research & Related Senior/Key Person Profile (Expanded) Form,
- Research & Related Budget Form,
- Research & Related Project/Performance Site Location(s), and
- R&R Subaward Budget Attachment(s), if applicable

All attachments that require signatures must be filled out, printed, signed, and scanned prior to being uploaded. All attachments should be PDF files, in accordance with the formatting guidelines specified for full proposal preparation.

1. SF 424 (R&R), Application for Federal Assistance Form. This form is required for each application. The form is self-explanatory, with the following exceptions: The **Applicant Identifier box** should be filled in with the the unique CDMRP Proposal Log Number, provided in the full proposal invitation letter. **Block 4 - Federal Identifier** box should be used to identify the Funding Opportunity number, which is W81XWH-06-GWVIRP.

2. Research & Related Other Project Information Form: The following information must be included as PDF file attachments to this form:

Blocks 1 - 5: This section is self-explanatory in addressing the use of human subjects, the use of animals, proprietary information, and environmental impact of the research.

Block 6: Technical and Public Abstracts and the Statement of Work: The technical and public abstracts (one-page limit each) and the Statement of Work (two-page limit) should be submitted in a single PDF file, in accordance with the formatting guidelines specified for full proposal preparation. Abstracts of all funded proposals will be posted on the CDMRP website at http://cdmrp.army.mil. Proprietary or confidential information should ***not*** be included in either the technical or the public abstract.

- **Technical Abstract: One-page limit.** Use the outline below when preparing the technical abstract.
  - Background: Present the ideas and reasoning behind the proposed work.
  - Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
  - Specific Aims: State the specific aims of the study.
  - Study Design: Briefly describe the study design including appropriate controls.

- Impact: Provide a brief statement explaining the impact of the proposed work to the identification of effective treatment interventions or potential treatment targets for Gulf War Illnesses.

- **Public Abstract: One-page limit.** Describe the scientific objective and rationale for the proposal in a manner readily understood by a non-scientifically trained audience.

- **Statement of Work: Two-page limit.** The Statement of Work is a concise restatement of the research proposal that outlines, step by step, how each major goal or objective of the proposed research/services will be accomplished during the period for which the USAMRMC will provide financial support. When a proposal requesting funding as part of a larger study is submitted, the proposal's Statement of Work must include DOD-funded tasks only.

Block 7: Project Narrative: Five-page limit for Exploration – Hypothesis Development Awards; 20-page limit for Investigator-Initiated Research Awards. The project narrative is the main body of the invited full proposal. The page limit for the project narrative is inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other relevant information needed to judge the proposal. The attachment should be a PDF file, in accordance with the formatting guidelines specified for full proposal preparation. The project narrative should reflect the intent and key features of the respective award mechanism and address the GWVIRP Program objectives and priority areas.

Block 8 – Bibliography & References Cited. No page limit.

- **References Cited:** List all relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate). The inclusion of Internet URLs to references is encouraged.

- **Acronyms and Symbol Definitions:** Starting on a new page titled "Acronyms and Symbol Definitions," provide a glossary of acronyms and symbols.

- **In Block 8, upload the two sections (References Cited and Acronyms and Symbol Definitions) as a single PDF file** in accordance with the formatting guidelines specified for full proposal preparation.

Block 9: Facilities & Other Resources. No page limit. Describe the facilities available for performance of the proposed request and any additional facilities or equipment proposed for acquisition at no cost to the USAMRMC. Indicate if Government-owned facility or equipment is proposed for use. Reference should be made to the original or present contract under which the facilities or equipment items are now accountable. There is no form for this information. The attachment should be a PDF file, in accordance with the formatting guidelines specified for full proposal preparation**.**

Block 10: Equipment: Include a description of existing equipment to be used for the proposed research project. There is no form for this information. The attachment should be a PDF file, in accordance with the formatting guidelines specified for full proposal preparation.

Block 11: Other Attachments. Submit only material specifically requested in this FY06 GWVIRP Supplement. Submit the attachments listed below. Attachments outlined in this section should be uploaded as separate PDF files in the following order. All attachments should be PDF files, in accordance with the formatting guidelines specified for full proposal preparation.

- **Publications and/or Patent Abstracts: Five-document limit.** Include up to five relevant publication reprints and/or patent abstracts. A patent abstract should provide a non-proprietary description of the patent application. A maximum of five publication reprints and/or patent abstracts is allowed; extra items will not be reviewed.
- **Letters of Institutional Support:** Provide signed letter(s) of institutional support that reflect the extent to which the PI will be relieved of academic or administrative responsibilities and allowed to pursue his or her research goals.
- **Letters from Collaborators:** Provide a signed letter from each collaborating individual or institution (if applicable).
- **Animal Use Summary (if applicable): Three-page limit.** If the proposed study involves animals, the applicant is ***required*** to submit a summary describing the animal subject research that will be conducted. Guidelines are provided in Attachment 2.
- **Human Use Research Review Summary (if applicable): Three-page limit.** If the proposed study involves human subjects, human data and/or human biological substances, the applicant is ***required*** to submit a maximum of three pages summarizing key aspects of human subjects research that will be conducted. Guidelines are provided in Attachment 3.
- **Federal Agency Financial Plan:** Proposals from Federal agencies ***must*** provide a plan delineating how all funds will be obligated by September 30, 2007, and how funds will be available to cover research costs over the entire award period. The plan must include the funding mechanism(s) that will be used to carry over funds between fiscal years, such as administrative agreements with foundations, non-Federal institutions, and universities.

Submitting material that was not requested may be construed as an attempt to gain a competitive advantage and such material will be removed; submitting such material may be grounds for administrative rejection of the proposal. The attachment should be a PDF file, in accordance with the formatting guidelines specified for full proposal preparation. ***This section is not intended for additional figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, or other information needed to judge the proposal.***

3. Research & Related Senior/Key Person Profile (Expanded) Form: Include the requested information for the PI and each senior/key person proposed on the project. The attachments should be a PDF file, in accordance with the formatting guidelines specified for full proposal preparation.

a. PI and Senior/Key Personnel Biographical Sketches: Four-page limit per individual. Suggested format is provided as Attachment 1 to this document**.**

b. **Current/Pending Support: Proposals submitted under this FY06 GWVIRP Supplement should not duplicate other funded research projects**. For all current and pending research projects involving the PI and senior/key personnel, include the title, time commitments, supporting agency, the name and address of the Procuring Contracting/Grants Officer, period of performance, and level of funding, *a brief description of the project's goals, and a list of the specific aims*. Provide justification for the requested support and interest where the projects overlap or parallel. If no current support exists, enter "None." The attachments should be PDF files, in accordance with the formatting guidelines specified for full proposal preparation. These data will be required to be updated during award negotiations.

4. Research & Related Budget Form: An estimate of the total research project cost, with a breakdown by category and year, must accompany each full proposal. All costs must be entered in U.S. dollars. Recipients performing outside of the U.S. should include the cost in local currency, the rate used for converting to U.S dollars and justification/basis for the conversion rate used.

A. Funding for an Exploration – Hypothesis Development Award ranges from $25,000 to $75,000 for direct costs over the performance period. The performance period may be requested for up to 1 year. Indirect costs should be added as appropriate. No more than $75,000 for direct costs will be granted in any single year during the lifetime of the award. Funds for this award may not be used for human subjects or specimens unless they are exempt under 32 CFR 219.101(b) (see Footnote 1, page 5) or eligible for expedited review (32 CFR 219.110; 21 CFR 56.110) (see Footnote 2, page 5).

B. Funding for an Investigator-Initiated Research Award ranges from $25,000 to $600,000 for direct costs over the performance period. The performance period may be requested for up to 4 years. Indirect costs should be added as appropriate. No more than $600,000 for direct costs will be granted in any single year during the lifetime of the award.

C. Maximum Obligation: The USAMRMC for support of this project shall not exceed the amount specified in the assistance agreement or as amended. The USAMRMC does not amend grants to provide additional funds for such purposes as reimbursement for unrecovered indirect costs resulting from the establishment of final negotiated rates or for increases in salaries, fringe benefits, and other costs.

D. Cost Regulations and Principles: Costs proposed must conform to the following regulations and principles:

1. Commercial Firms: Federal Acquisition Regulations (FAR) Part 31 and Defense FAR Supplement Part 31, (http://farsite.hill.af.mil) Contract Cost Principles and Procedures.

2. Educational Institutions: OMB Circular A-21, Cost Principles for Educational Institutions.

3. Nonprofit Organizations: OMB Circular A-122, Cost Principles for Nonprofit Organizations. OMB Circular A-133, Audits of Institutions of Higher Education and Other Nonprofit Organizations.

4 State, Local and Tribal Governments: OMB Circular A-87, Cost Principles for State, Local, and Indian Tribal Governments.

5. Cost of Preparing Proposals: The cost of preparing proposals in response to this FY06 GWVIRP Supplement is not considered an allowable direct charge to any resultant contract, grant or cooperative agreement. It is, however, an allowable expense to the bid and proposal indirect cost specified in FAR 31.205-18, and OMB Circulars A-21 and A-122.

Section A & B – Senior/Key Person: The basis for labor costs should be predicated upon actual labor rates or salaries. Budget estimates may be adjusted upward to forecast salary or wage cost-of-living increases that will occur during the period-of-performance. The proposal should separately identify and explain the ratio applied to base salary/wage for cost-of-living adjustments and merit increases in the budget justification (Section K).

The qualifications of the PI and the amount of time that he or she and other professional personnel will devote to the research are important factors in selecting research proposals for funding. For each key staff member identified on the Research & Related Budget Form, list the percentage of each appointment to be spent on this project.

Section C – Equipment Description: It is DOD policy that all commercial and nonprofit recipients provide the equipment needed to support proposed research. In those rare cases where specific additional equipment is approved for commercial and nonprofit organizations, such approved cost elements shall be separately negotiated.

An itemized list of permanent equipment is required, showing the cost for each item. Permanent equipment is any article of nonexpendable tangible property having a useful life of more than 2 years and an acquisition cost of $5,000 or more per unit. The justification for the cost of each item of equipment included in the budget must be disclosed in the budget justification (Section K) to include:

(1) Vendor Quote: Show name of vendor and number of quotes received and justification if intended award is to other than the lowest bidder.

(2) Historical Cost: Identify vendor, date of purchase and whether or not cost represented the lowest bid. Include reason(s) for not soliciting current quotes.

(3) Estimate: Include rationale for estimate and reasons for not soliciting current quotes.

(4) Special test equipment to be fabricated by the contractor for specific research purposes and its cost.

(5) Standard equipment to be acquired and modified to meet specific requirements, including acquisition and modification costs, listing separately.

(6) Existing equipment to be modified to meet specific research requirements, including modification costs. Do not include as special test equipment those items of equipment that, if purchased by the contractor with contractor funds, would be capitalized for Federal income tax purposes.

(7) Title of equipment or other tangible property purchased with Government funds may be vested in institutions of higher education or with nonprofit organizations whose primary purpose is the conduct of scientific research. Normally the title will vest in the recipient if vesting will facilitate scientific research performed by the institution or organization for the Government.

(8) Commercial organizations are expected to possess the necessary plant and equipment to conduct the proposed research. Equipment purchases for commercial organizations will be supported only in exceptional circumstances.

Section D – Travel: Costs for travel include:

- **Travel costs to attend one scientific/technical meeting per year.** Costs should not exceed $1,800.
- **Travel costs associated with the execution of the proposed work.** If applicable, reasonable costs for travel between collaborating institutions should be included and are not subject to the yearly $1,800 limitation on travel to meetings. Justification for these travel costs should be provided. Travel outside the U.S. requires prior approval from the US Army Medical Research Acquisition Activity.
- **Travel to CDMRP-Related Meeting**. PIs will be invited to present their results at the next CDMRP Military Health Research Forum. Travel funds should not exceed $1,800 for this meeting. If the award has expired before the meeting is held, funding will be made available for PIs to participate in the meeting. It is anticipated that the next Military Health Research Forum will be held in May 2008.

Section E – Participant/Trainee Support Costs: This section is self-explanatory.

Section F – Other Direct Costs

Section F.1 – Materials and Supplies (Consumables): The justification (to be included in Section K) supporting materials and supplies (consumable) costs should include a general description of expendable equipment and supplies. If animals are to be purchased, state the species, strain (if applicable) and the number to be used. If human cell lines are to be purchased, state the source and the description.

Section F.2 – Publication Costs: This section is self-explanatory.

Section F.3 – Consultant Services: Regardless of whether funds are requested, the justification (to be included in Section K) should include the names and organizational affiliations of all consultants. State the daily consultant fee, travel expenses, nature of the consulting effort, and why consultants are required for the proposed research project.

Section F.4 – ADP/Computer Services: This section is self-explanatory.

Section F.5 – Subaward/Consortium/Contractual Costs: Enter the total funds requested for (1) all subaward/consortium organization(s) proposed for the project and (2) any other contractual costs proposed for the project.

Section F.6 – Equipment or Facility Rental/User Fees: This section is self-explanatory.

Section F.7 – Alterations and Renovations: Not allowable.

Section F (8 – 10) – Research-Related Subject Costs: Include itemized costs of subject participation in the research study. These costs are strictly limited to expenses specifically associated with the proposed study. The USAMRMC will not provide funds for ongoing medical care costs that are not related to a subject's participation in the research study.

Section F (8 – 10) – Other Direct Costs: Include other anticipated direct costs that are not specified elsewhere in the budget. Unusual or expensive items should be fully explained and justified in Section K.

Section G – Direct Costs: This section is self-explanatory.

Section H – Indirect Costs (overhead, general and administrative, and other): The most recent rates, dates of negotiation, base(s) and periods to which the rates apply should be disclosed along with a statement identifying whether the proposed rates are provisional or fixed. If negotiated forecast rates do not exist, provide sufficient detail in the budget justification (Section K) regarding a determination that the costs included in the forecast rate are allocable according to applicable FAR/DFARS or OMB Circular provisions. Commercial firms can also visit www.dcaa.mil for additional information on indirect rates. Disclosure should be sufficient to permit a full understanding of the content of the rate(s) and how it was established.

As a minimum, justification for indirect costs should identify:

a. All individual cost elements included in the forecast rate(s);
b. The basis used to prorate indirect expenses to cost pools, if any;
c. How the rate(s) was calculated; and
d. The distribution basis of the developed rate(s).

Section I – Total Direct and Indirect Costs: This section is self-explanatory.

Section J – Fee: A profit or fixed fee is not allowable on grants or cooperative agreements. If a profit/fee is negotiated, a contract will be awarded. Any fixed fee applied to the research project must be listed and any claimed Facilities Capital Cost of Money supported by **DD Form 1861** (www.dtic.mil/whs/directives/infomgt/forms/forminfo/forminfopage2192.html) submitted with the full proposal.

Section K – Budget Justification: The Budget Justification must be included as an attachment at Research & Related Budget – Section K for each research period. The attachment should be a PDF file, in accordance with the formatting guidelines specified for full proposal preparation. Organizations must provide sufficient detail and justification so that the Government can determine the proposed costs to be allocable and reasonable for the proposed research effort. Attach one PDF file that addresses each of the cost elements proposed.

5. Research & Related Project/Performance Site Location(s): Indicate the primary site where the work will be performed. If a portion of the work will be performed at any other site(s), include the name and address for each collaborating location in the data fields provided. If more than eight performance site locations are proposed, provide the requested information in a separate file and attach to this form.

6. R&R Subaward Budget Attachment(s) Form, if applicable: On this form, attach all subaward budget file(s) for this application.

Complete the subawardee budget(s) using the Research & Related Subaward Budget in accordance with the instructions. Please note that the files to be attached to the R&R Subaward Budget Attachment(s) Form must be PureEdge documents (instructions on installing PureEdge Viewer, a free software program, can be found on Grants.gov).

The Budget Justification for each subaward must be included as an attachment at Research & Related Budget – Section K of each subaward budget. A description of services or materials that are to be awarded by subcontract or subgrant is required. Organizations must provide sufficient detail and justification so that the Government can determine the proposed costs to be allocable and reasonable for the proposed research effort. The following information must be provided on subawards totaling $10,000 or more:

a. Identification of the type of award to be used (e.g., cost reimbursement, fixed price);

b. Identification of the proposed subcontractor or subgrantee, if known, and an explanation of why and how the subcontractor or subgrantee was selected or will be selected;

c. Whether the award will be competitive and, if noncompetitive, rationale to justify the absence of competition;

d. The proposed acquisition price; and

e. The PI's cost or price analysis for the subgrant or subcontract proposed price (applicable only if the award exceeds $500,000).

If the resultant award is a contract that exceeds $500,000 and the offer or is a large business or an educational institution (other than HBCU/MI), the contractor is required to submit a subcontracting plan for small business and small disadvantaged business concerns, in accordance with FAR 19.7. A mutually agreeable plan will be incorporated as part of the resultant contract.

VII. FULL-PROPOSAL FORMAT AND COMPLIANCE GUIDELINES

A. Proposal Format: The proposal must be clear and legible and conform to the formatting guidelines described below. The font size, spacing, page size, and margins may differ between the word processing, PDF, and printed versions. These guidelines apply to the document properties of the electronic version of the PDF file(s) as viewed on a computer screen.

- **Document Format:** All attachments must be PDF files.
- **Font Size:** 12 point or larger.
- **Font Type:** Times New Roman is strongly recommended.
- **Spacing:** No more than six lines of type within a vertical inch (2.54 cm).
- **Page Size:** No larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- **Margins:** Must be at least 0.5 inch (1.27 cm) in all directions.
- **Print Area:** 7.5 inches x 10.0 inches (approximately 19.05 cm x 25.40 cm).
- **Color, High-Resolution, and Multimedia Objects:** Proposals may include color, high-resolution, or multimedia objects (e.g., MPEG, WAV, or AVI files) embedded in the PDF files; however, these objects must not exceed 15 seconds in length and a size of 10 MB. Since some reviewers work from black and white printed copies, PIs may wish to include text in the proposal directing the reviewer to the electronic file for parts of the proposal that may be difficult to interpret when printed in black and white. Photographs and illustrations must be submitted in JPEG format; bit map or TIFF formats are not allowed.
- **Internet URLs:** URLs directing reviewers to websites containing additional information about the proposed research are not allowed in the proposal or its components. Inclusion of such URLs may be perceived as an attempt to gain an unfair competitive advantage. Links to publications referenced in the proposal are encouraged.
- **Language:** English.
- **Headers and Footers:** Should not be used.
- **Page Numbering:** Should not be used.

B. Administrative Compliance Issues: Compliance guidelines have been designed to ensure the presentation of all proposals in an organized and easy-to-follow manner. Peer reviewers expect to see a consistent, prescribed format for each proposal. ***Failure to adhere to format requirements makes proposals difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in proposal rejection.***

The following ***will*** result in administrative rejection of the entire proposal before it reaches peer review:

- All attached files are not PDF files.
- Project narrative exceeds page limit.
- Project narrative is missing.
- Required supporting documentation is missing including:
  - Letter(s) of institutional support
  - Letter(s) of collaboration (in cases involving collaborations between two or more institutions).
- Budget justification is missing.
- Project Narrative is incomplete after the deadline.
- Inclusion of GWVIRP IP members in any capacity in the invited full proposal process, including the budget and any supporting documentation. A list of the FY06 GWVIRP IP members may be found at http://cdmrp.army.mil/prmrp/default.htm.
- Required animal use and/or human biological substances and human subject's research review summaries are missing.
- Federal Agency Financial Plan is not included (if applicable).

For any other sections of the proposal with a defined page limit, pages exceeding the specified limit will be removed from the proposal and not forwarded for peer review.

Material submitted after the proposal submission deadline, unless specifically requested by the Government, will not be forwarded for peer review.

VIII. FULL PROPOSAL REVIEW INFORMATION

A. Proposal Review and Selection Overview: Proposals are evaluated using a two-tier review process. The first tier is a scientific peer review of proposals against established criteria for determining scientific merit. The second tier is a programmatic review that compares submissions to each other and recommends proposals for funding based on scientific merit and overall goals of the Program.

B. Peer Review

1. Process: Peer review is conducted by scientific reviewers and survivors of the 1991 Gulf War diagnosed with a GWI. These Gulf War survivors will be referred to as consumers in the remainder of this document. The primary responsibility of the peer reviewers is to provide unbiased, expert advice on the scientific/technical merit and relevance of proposals based on the review criteria published for each award mechanism.

Scientific reviewers are selected for their subject matter expertise and experience with scientific peer review. Consumer reviewers are nominated by an advocacy or support organization and are selected on the basis of their leadership skills, commitment to advocacy, and interest in corresponding science. Consumers augment the peer review process by bringing the patient perspective to the assessment of science and the relevance of the research.

The proposal and appropriate supporting documentation are used by reviewers during the peer review process.

The peer review summary statement is a product of scientific peer review. Each summary statement includes the peer review scores and an evaluation of the project as assessed by the peer reviewers according to the evaluation criteria published in this document.

2. Review Criteria

a. Exploration – Hypothesis Development Award

- **Innovation and Novelty of Concept:** ***This is the most highly weighted review criterion for this award mechanism, and thus it contributes more than the other criteria to the global priority score.***
  - How the proposal addresses an untested or unexplored problem or question in GWI research, or looks at an existing problem or question from a new and untested perspective.
  - How the proposed research is innovative in concept or question, research methods or technologies, adaptations of existing methods or technologies, or other ways.
  - How the project proposes new paradigms or challenges existing paradigms.
  - How the proposed research represents more than a mere extension or an incremental advance upon published data.
  - How the intended results should give rise to a testable hypothesis.
- **Impact**
  - How the proposal addresses an important problem and directly addresses the selected FY06 GWVIRP priority area.
  - How scientific knowledge will be advanced if the aims of the application are achieved.
  - How these studies will affect the concepts or methods that drive this field.

- **Plausibility and Feasibility**
  - How the scientific rationale supports the project and its feasibility as demonstrated by a critical review and analysis of the literature and logical reasoning.
  - How the concepts, experimental design, methods, and analyses support the plausibility and feasibility of the proposed work.
  - How well the PI acknowledges potential problems and addresses alternative approaches.
- **PI and Key Personnel Qualifications**
  - How the experience and expertise of the PI and other researchers (if any) is appropriate to the work proposed.
  - Appropriateness of the levels of effort by the PI and other key personnel to ensure the success of this project.
  - Conversely, whether the PI and key personnel are overcommitted on other funded studies.
  - How collaborations that have been developed will support the goals of the project and whether letters have been submitted to demonstrate support.
- **Facilities**
  - The appropriateness of the scientific environment for the proposed research.
  - How the research requirements are adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed.
  - Whether there is evidence of adequate institutional support (space and equipment) provided with the proposal.
- **Animal Research Review Summary (if applicable)**
  - How the PI addressed the issues listed in the Animal Research Review Summary document (Attachment 2).
- **Human Use Research Review Summary (if applicable)**
  - How the PI addressed the issues listed in the Human Use Research Review Summary (information regarding human biological substances, human data and human subjects) (Attachment 3)**.**
- **Budget**
  - How the budget is justified and appropriate for the research proposed.
  - Whether any recommended or required changes need to be made for personnel, travel, supplies, consultants, equipment costs, or the scope of the research (time or aims).

- Whether arrangements have been made, where appropriate, to compensate human subjects/participants for expenses they incur from participating in the project.

b. Investigator-Initiated Research Award

- **Research Strategy and Objectives**
  - How the hypotheses, experimental design, rationale, methods, and analyses are developed and appropriate for, and well integrated into, the aims of the project.
  - How the proposed research represents more than a slight extension or repeat of currently funded research.
  - How the PI acknowledges potential problem areas and considers alternative methods/tactics.
- **Impact**
  - How the proposal addresses an important problem and directly addresses one or both FY06 GWVIRP priority areas.
  - How scientific knowledge will be advanced if the aims of the application are achieved.
  - How these studies will affect the concepts or methods that drive this field.
  - Whether the results are likely to be published in the peer-reviewed scientific literature.
- **PI and Key Personnel Qualifications**
  - How the experience and expertise of the PI and other researchers (if any) is appropriate to the work proposed.
  - Appropriateness of the levels of effort by the PI and other key personnel to ensure the success of this project.
  - Conversely, whether the PI and key personnel are overcommitted on other funded studies.
  - Whether conflicts of interest and commercial interests are adequately identified and justified (if applicable).
  - How collaborations (if any) that have been developed will support the goals of the project and whether letters have been submitted to demonstrate support.
- **Facilities**
  - The appropriateness of the scientific environment for the proposed research.
  - How the research requirements are adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed.

- Whether there is evidence of adequate institutional support (space and equipment) provided with the proposal.

- **Animal Research Review Summary (if applicable)**
  - How the PI addressed the issues listed in the Animal Research Review Summary document (Attachment 2).

- **Human Use Research Review Summary (if applicable)**
  - How the PI addressed the issues listed in the Human Use Research Review Summary (information regarding human biological substances, human data and human subjects) (Attachment 3)**.**

- **Budget**
  - How the budget is justified and appropriate for the research proposed.
  - Whether any recommended or required changes need to be made for personnel, travel, supplies, consultants, equipment costs, or the scope of the research (time or aims).
  - Whether arrangements have been made, where appropriate, to compensate human subjects/participants for expenses they incur from participating in the project.

C. Programmatic Review

1. Process: Programmatic review is conducted by an IP, which is composed of scientists, clinicians, and a consumer. The scientific members of the IP represent diverse disciplines and specialty areas, and the consumer members represent those impacted by GWI. A function of programmatic review is to structure a broad portfolio of grants which are aligned with the programmatic priorities of the GWVIRP. Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool.

2. Review Criteria: Programmatic reviewers use the following criteria to assist in making their recommendations:

- Peer review recommendations
- Relevance/alignment to priority area(s)
- Congressional guidance
- VA priorities
- Budget
- Federal Agency Financial Plan (if applicable)
- Animal Research Review Summary (if applicable)
- Human Use Research Review Summary (if applicable)

Scientifically sound proposals that best fulfill the above peer and programmatic review criteria and most effectively address the unique focus and goals of the GWVIRP will be recommended to the Commanding General, USAMRMC, for funding.

IX. APPENDICES

APPENDIX 1

GRANTS.GOV INSTRUCTIONS

A. PUBLIC LAW 106-107

The Federal Financial Assistance Management Improvement Act of 1999, also known as Public Law 106-107 (P.L. 106-107), was enacted on November 1999. The purposes of the Act are to (1) improve the effectiveness and performance of Federal financial assistance programs, (2) simplify Federal financial assistance application and reporting requirements, (3) improve the delivery of services to the public, and (4) facilitate greater coordination among those responsible for delivering services.

B. GRANTS.GOV

Grants.gov is an E-Government initiative to provide a simple, unified electronic storefront for interactions between Principal Investigators (PIs) and the Federal agencies that manage grant funds. The grant community, including state, local and tribal governments, academia and research institutions, commercial firms and not-for-profits, can access the annual grant funds available across the Federal government through one website, Grants.gov. In addition to simplifying the grant application process, Grants.gov also creates avenues for consolidation and best practices within each grant-making agency.

In compliance with P.L. 106-107, the US Army Medical Research and Materiel Command requires proposals submitted in response to the FY06 GWVIRP Supplement to be submitted through Grants.gov APPLY. This requires that Organizations register in Grants.gov to submit proposals through the Grants.gov portal. Individual PIs/Project Directors DO NOT register; however, the Authorized Organization Representative (AOR) is required to register. The registration process can take several weeks, so please register as soon as possible.

The following actions are required as part of the registration process. If you do business with the Federal government on a continuing basis, it is likely you have already completed some of the actions, e.g., obtaining a DUNS number or registration in CCR. Detailed information, automated tools, and checklists are available at http://www.grants.gov/PIs/get_registered.jsp.

DUNS Number

An organization will need a Data Universal Number System (DUNS) Number. A DUNS number is a unique nine-character identification number provided by the commercial company Dun & Bradstreet (D&B). If an organization does not have a DUNS number, an authorized official of the organization can request one by calling 1-866-705-5711or online via web registration. Organizations located outside of the United States, can request and register for a DUNS number online via web registration.

Central Contractor Registry (CCR)

An organization must be registered with CCR before submitting a grant application through Grants.gov or receiving an award from the Federal Government. CCR validates PI information and electronically shares the secure and encrypted data with Federal agencies' finance offices to facilitate paperless payments through Electronic Funds Transfer.

You can register by calling the CCR Assistance Center at 1-888-227-2423 or register online at http://www.ccr.gov. If you have the necessary information, online registration will take about 30 minutes to complete, depending upon the size and complexity of your organization.

Authorized Organizational Representative (AOR)

Before submitting a proposal, an organization representative needs to register to submit on behalf of the organization at grants.gov - https://apply.grants.gov/OrcRegister. An organization's E-Business point of contact (POC), identified during CCR Registration, must authorize someone to become an AOR. This safeguards the organization from individuals who may attempt to submit proposals without permission. **Note: In some organizations, a person may serve as both an E-Business POC and an AOR.**

An AOR must first register with the Grants.gov credential provider at https://apply.grants.gov/OrcRegister and then with Grants.gov. Once an AOR has completed the Grants.gov process, Grants.gov will notify the E-Business POC for assignment of user privileges. When an E-Business POC approves an AOR, Grants.gov will send the AOR a confirmation email.

APPENDIX 2

AWARD ADMINISTRATION INFORMATION

A. Award Notices: Each Principal Investigator (PI) will receive notification of the award status of his or her proposal. A copy of the peer review summary statement will be posted to the Congressionally Directed Medical Research Programs (CDMRP) eReceipt system. PIs can expect to receive this notification approximately four weeks after programmatic review.

B. Administrative Requirements: Awards are made to organizations, not individuals. The PI must submit a proposal through, and be employed by or affiliated with, a university, college, nonprofit research institution, commercial firm, or Government agency (including military laboratories) to receive support. A prospective recipient must meet certain minimum standards pertaining to institutional support, financial resources, record of performance, integrity, organization, experience, operational controls, facilities, and conformance with safety and environmental statutes and regulations (OMB Circular A-110 and DOD Grant and Agreement Regulations) to be eligible for an award. Any organization requesting receipt of an award through this FY06 GWVIRP Supplement must be registered in the Central Contractor Registration (CCR) database. Access to the CCR online registration is through the CCR homepage at http://www.ccr.gov.

A change in PI is not allowed for the Exploration – Hypothesis Development or the Investigator-Initiated Award mechanism. A change in institutional affiliation will require the investigator to resubmit the entire proposal packet through his or her new institution to include any regulatory documentation that may require protocols, etc. to be approved for the new institution. The investigator's original institution must agree to relinquish the award. Any delay in the submission of the new information will result in a delay in contracting, regulatory review, and a subsequent delay in resuming work on the project.

C. Award Negotiation: Award negotiation consists of discussions, reviews, and justifications of critical issues involving the US Army Medical Research Acquisition Activity (USAMRAA). A Contract Specialist and/or representative from the USAMRAA will contact the Contract Representative authorized to negotiate contracts and grants at the PI's institution. Additional documentation and justifications related to the budget may be required as part of the negotiation process.

The award start date will be determined during the negotiation process.

D. Disclosure of Proprietary Information outside the Government: By submitting a proposal, the PI understands that proprietary information may be disclosed outside the Government for the sole purpose of technical evaluation. The US Army Medical Research and Materiel Command (USAMRMC) will obtain a written agreement from the evaluator that proprietary information in the proposal will only be used for evaluation purposes and will not be further disclosed or used. Funded proposals may be subject to public release under the Freedom of Information Act; proposals that are not selected for funding are not subject to public release.

E. Government Obligation: PIs are cautioned that only an appointed Contracting/Grants Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government to fund preparation of a proposal or to support research should be inferred from discussions with a technical project officer. PIs who, or organizations that, make financial or other commitments for a research effort in the absence of an actual legal obligation signed by the USAMRAA Contracting/Grants Officer do so at their own risk.

F. Information Service: PIs may use the technical reference facilities of the National Technical Information Service, 5285 Port Royal Road, Springfield, Virginia 22161, for the purpose of surveying existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. All other sources also should be consulted to the extent practical for the same purpose.

G. Inquiry Review Panel: PIs may submit a letter of inquiry to the USAMRMC in response to funding decisions made for a given proposal. Members of the CDMRP staff, the USAMRMC Judge Advocate General staff, and USAMRAA Grants Officers constitute an Inquiry Review Panel and review each inquiry to determine whether factual or procedural errors in either peer or programmatic review have occurred, and if so, what action should be taken.

H. Title to Inventions and Patents: In accordance with the Bayh-Dole Act (35 USC 200 et seq.[1]), title to inventions and patents resulting from such Federally funded research may be held by the grantee or its collaborator, but the US Government shall, at a minimum, retain nonexclusive rights for the use of such inventions. An investigator must follow the instructions in the assistance agreement concerning license agreements and patents.

I. J-1 Visa Waiver: It is the responsibility of the awardee to ensure that the research staff is able to complete the work without intercession by the DOD for a J-1 Visa Waiver on behalf of a foreign national in the United States under a J-1 Visa.

[1] Title 35, United States Code, Sections 200 et seq.

APPENDIX 3

REGULATORY REQUIREMENTS AND REVIEWS

The Principal Investigator (PI) may not use, employ, or subcontract for the use of any human subjects, human biological substances, cadavers, or laboratory animals until applicable regulatory documents are requested, reviewed, and approved by the US Army Medical Research and Materiel Command (USAMRMC).

Concurrent with the US Army Medical Research Acquisition Activity (USAMRAA) negotiation, the Office of Surety, Safety and Environment will review the Certificate of Environmental Compliance and the Principal Investigator Safety Program Assurance form to be submitted upon request. The applicable USAMRMC regulatory office will review documents related to research involving animal use, human subjects/anatomical substance use, and cadaver use also to be submitted upon request to ensure that Department of Defense (DOD) regulations are met.

1. Certificate of Environmental Compliance: The Certificate of Environmental Compliance will be requested at award negotiations. If multiple research sites/institutions are funded in the proposal, then a Certificate of Environmental Compliance for each site will also be requested.

2. Safety Program Documents: The Principal Investigator Safety Program Assurance form will be requested at award negotiations.

A Facility Safety Plan is required; it will be requested at award negotiations. A Facility Safety Plan from the PI's institution may have been received previously and approved by the USAMRMC. A list of institutions that have approved Facility Safety Plans can be found on the USAMRMC website at https://mrmc.detrick.army.mil/crprcqsohdfsplan.asp. If the PI's institution is not listed on the website, contact the institution's Facility Safety Director/Manager to initiate completion of the institution-based Facility Safety Plan. Specific requirements for the Facility Safety Plan can be found at https://mrmc.detrick.army.mil/docs/rcq/FY02FSPAppendix.doc.

If multiple research sites/institutions are funded in the proposal, a Facility Safety Plan for each site/institution not listed in the aforementioned website will be requested at a later date.

3. Research Involving Animal Use (*This section is not related to the Animal Research Review Summary referenced in Attachment 2*.): Specific documents relating to the use of animals in the proposed research will be requested by the Congressionally Directed Medical Research Programs (CDMRP) if the proposal is selected for funding (these documents should not be submitted with the proposal). The Animal Care and Use Review Office (ACURO), a component of the USAMRMC Office of Research Protections (formerly Regulatory Compliance and Quality), must review and approve all animal use prior to the start of working with animals. PIs must complete and submit the animal use appendix titled "Research Involving Animals," which can be found on the ACURO website

https://mrmc-www.army.mil/rodorpaurd.asp). Allow 2 months for regulatory review and approval processes for animal studies.

Specific requirements for research involving animals can be found at https://mrmc.detrick.army.mil/docs/rcq/FY05AnimalAppendix.doc.

4. Research Involving Human Subjects/Biological Substances/Cadavers (*This section is not related to the Human Use Research Review Summary referenced in Attachment 3.*):
Documents related to the use of human subjects or substances or cadavers will be requested by the CDMRP if the proposal is selected for funding (these documents should not be submitted with the proposal). In addition to local Institutional Review Board (IRB) approval to conduct research involving human subjects and/or biological substances or cadavers, a second tier of human subjects regulatory review and approval is also required by the DOD. This second review is conducted by the USAMRMC Office of Research Protections, Human Research Protection Office (HRPO). The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed and will require information in addition to that supplied to the local review board. Allow 4 to 6 months for regulatory review and approval processes for human use studies.

a. Requirements: Specific requirements for research involving human subjects, human biological substances, and/or cadavers can be found at https://mrmc.amedd.army.mil/rodorptoolkit.asp.

Personnel involved in human subjects research must have appropriate instruction in the protection of human subjects. Documentation confirming that this instruction has been completed will be required during the regulatory review process.

It is expected that there will be timely resolutions of human subjects protocols submitted to the investigator's local IRB.

Additional information pertaining to the human subjects regulatory review process, guidelines for developing protocols, and suggested language for specific issues can be found at: https://mrmc.detrick.army.mil/rodorphrpo.asp.

b. Informed Consent Form: An informed consent form template is located at https://mrmc.detrick.army.mil/docs/rcq/Proconsent/ConsentFormGuidelines.doc.

c. Intent to Benefit: Investigators must consider the requirements of Title 10 United States Code Section 980 (10 USC 980) applicable to DOD-sponsored research before writing a research protocol. Title 10 United States Code Section 980 requires that "Funds appropriated to the Department of Defense may not be used for research involving a human being as an experimental subject unless (1) the informed consent of the subject is obtained in advance; or (2) in the case of research intended to be beneficial to the subject, the informed consent may be obtained from a legal representative of the subject."

Furthermore and consistent with the Common Federal Policy for the Protection of Human Subjects, if an individual cannot give his or her own consent to participate in a research study, consent of the individual's legally authorized representative must be obtained before the individual's participation in the research. Moreover, an individual not legally competent to consent (e.g., incapacitated individuals, incompetents, minors) may not be enrolled in a DOD-supported experiment unless the research is intended to benefit each subject enrolled in the study. For example, a subject may benefit directly from medical treatment or surveillance beyond the standard of care. Investigators should be aware that this law makes placebo-controlled clinical trials problematic because of the "intent to benefit" requirement whenever participation is sought of subjects from whom consent must be obtained by the legally authorized representative.

d. Conditions Regarding DOD Funding of Research on Human Embryonic Stem Cells: Research involving the derivation and use of human embryonic germ cells from fetal tissue may be conducted with DOD support ***only*** when the research is in compliance with 45 CFR 46, Subpart B (Title 45 of the Code of Federal Regulations, Section 46, Subpart B); 42 USC 289g through 289g-2; US Food and Drug Administration regulations; and any other applicable Federal, state, and local laws and regulations.

Research on existing human embryonic stem (hES) cell lines may be conducted with Federal support through the DOD ***only*** if the cell lines meet the current US Federal criteria as listed on the following National Institutes of Health (NIH) website (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html). A list of the currently approved cell lines can be obtained from the NIH Human Embryonic Stem Cell Registry (http://stemcells.nih.gov/research/registry). The NIH code should be used to identify the cell lines in the proposal.

Research involving the derivation of new stem cells from human embryos or the use of hES cells that are not listed on the NIH Human Embryonic Stem Cell Registry may not be conducted with Federal support through the DOD.

This restriction applies to hES cells derived from blastocysts remaining after infertility treatments and donated for research, blastocysts produced from donated gametes (oocytes and sperm) for research purposes, and the products of nuclear transfer. The research is subject to all applicable local, state, and Federal regulatory requirements.

e. Clinical Trial Registry: All PIs are required to register clinical trials individually on www.clinicaltrials.gov using a Secondary Protocol ID number designation of: CDMRP-CDMRP Log Number. If several protocols exist under the same proposal, the Secondary Protocol ID number must be: CDMRP-CDMRP Log Number-A, B, C, etc. ***Clinical trials must be registered prior to enrollment of the first patient.*** All trials that meet the definition on the NIH database (see http://prsinfo.clinicaltrials.gov/, click on "Data Element Definitions," see section 6, "Study Phase" and "Study Type") including all Phase I-IV clinical trials and trials that do not fit into one or more phases, but that are clearly interventional or observational (e.g., some epidemiological or behavioral studies) are required to register.

APPENDIX 4

REPORTING REQUIREMENTS

The Government requires reports to be submitted for continuation of the research and funding. The specific reports due to the Government will be described in each award instrument. (Full US Army Medical Research and Materiel Command reporting requirements can be found at https://mrmc-www.army.mil, under "Links and Resources.") ***Failure to submit required reports by the required date may result in a delay in or termination of award funding.***

Reporting requirements include the following:

1. Research Progress Reports: Reporting requirements consist of an annual report (for each year of research except the final year) that presents a detailed summary of scientific issues and accomplishments and a final report (submitted in the last year of the award period) that details the findings and issues for the entire project. Copies of all publications and patent applications resulting from Congressionally Directed Medical Research Programs funding should be included in the progress report.

2. Fiscal Reports: Quarterly fiscal report requirements may include the Standard Form Report, SF 272, Federal Cash Transaction, used for grants and cooperative agreements to track the expenditure of funds on the research project.

3. Non-Exempt Human Studies Reports: For non-exempt human subjects research, documentation of local Institutional Review Board (IRB) continuing review (in the intervals specified by the local IRB but at least annually) and approval for continuation must be submitted directly to Office of Research Protections – Human Research Protection Office.

4. Animal Use Reports: Principal Investigators are required to submit annual animal use information for a report to Congress, verification of annual protocol review, and notification of protocol suspension or revocation. Institutions are required to provide updated US Department of Agriculture reports and notification of changes to accreditation status as verified by the Association for Assessment and Accreditation of Laboratory Animal Care International, and the Office of Laboratory Animal Welfare.

APPENDIX 5

ACRONYM LIST

ACURO	Animal Care and Use Research Office
AOR	Authorized Organizational Representative
AVI	Audio Video Interleave
CCR	Central Contractor Registration
CDMRP	Congressionally Directed Medical Research Programs
CFDA	Catalog of Federal Domestic Assistance
CFR	Code of Federal Regulations
COI	Conflicts of Interest
CR	Contract Representative
DOD	Department of Defense
DODGAR	Department of Defense Grant and Agreement Regulations
DUNS	Data Universal Number System
EPLS	Excluded Parties List System
FAR	Federal Acquisition Regulations
FY	Fiscal Year
GWVIRP	Gulf War Veterans' Illnesses Research Program
HBCU/MI	Historically Black Colleges and Universities/Minority Institutions
hES	Human Embryonic Stem
HRPO	Human Research Protection Office
IP	Integration Panel
IRB	Institutional Review Board
M	Million
MB	Megabyte
MPEG	Moving Picture Experts Group
NIH	National Institutes of Health
OMB	Office of Management and Budget
PI	Principal Investigator
P.L.	Public Law
POC	Point of Contact
R&R OPI	Research & Related Other Project Information
USAMRAA	US Army Medical Research Acquisition Activity
USAMRMC	US Army Medical Research and Materiel Command
USC	United States Code
VA	Department of Veterans Affairs
WAV	Waveform Audio

X. ATTACHMENTS

ATTACHMENT 1

BIOGRAPHICAL SKETCH TEMPLATE

Provide the following information for each individual included in the Research & Related Senior/Key Person Profile (Expanded) Form.			
NAME	POSITION TITLE		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training).			
INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List in chronological order, the titles, all authors and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds 2 pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED 4 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INDIVIDUAL.

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY.
DO NOT EXCEED 4 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INDIVIDUAL.

ATTACHMENT 2

ANIMAL RESEARCH REVIEW SUMMARY GUIDELINES

When the proposed study involves animals, the applicant is ***required*** to submit a summary (***three-page limit***) describing the animal subject research that will be conducted. The following points must be addressed:

- **Objective of Research**
  - Briefly describe the purpose/research objective of the animal study
- **Rationale for Using Animals, to include:**
  - Species identification
  - Number of animals (with justification)
- **Brief Summary of Procedures, to include:**
  - Veterinary care
  - Pain alleviation
  - Euthanasia
- **Summary of Control Model(s)**
- **Brief Summary of Proposed Timeline, to include access to animals**
- **Brief Summary of Research Requiring BSL3/4 Containment**
- **Contact Information for the Institutional Animal Care and Use Committee (IACUC) Point of Contact**
- **Letter from the IACUC Stating that the Review Has Taken Place and Is Approved**

ATTACHMENT 3

HUMAN USE RESEARCH REVIEW SUMMARY GUIDELINES

If the proposed study involves ***human subjects***, ***human data***, and/or ***human biological*** substances, the applicant is ***required*** to submit a maximum of three pages summarizing key aspects of human use research that will be conducted. In particular, the following points must be addressed by Principal Investigators submitting full proposals to the Investigator-Initiated Award mechanism. PIs submitting full proposals to the Exploration-Hypothesis Development Award mechanism should address only the points that are applicable to exempt status under 32 CFR 219.101(b) (Title 32, Code of Federal Regulations, Section 219.101(b)) or that verify eligibility for expedited review (32 CFR 219.110; 21 CFR 56.110[1]).

a. Human Subjects

- **Objective of Study**
  - Briefly describe the purpose/research objective of the study.
- **Brief Summary of Procedure with Timeline**
  - Describe how the key study variables will be measured.
  - Describe the timeline for required study subject visits and list the procedures to be performed at each.
  - Briefly describe the procedures for data and specimen collection, analysis, and evaluation.
- **Proposed Subject Recruitment Process**
  - Describe the target population from which study subjects will be recruited.
  - Provide a scientific rationale for the target sample size.
  - Describe the subject recruitment process, including who will identify potential subjects and how they will be recruited.
- **Proposed Consent Process**
  - Describe the consent process, including when and where the consent interview will take place and the time available for the subjects to consider participation and ask questions.
  - Describe the circumstances under which consent from a legally authorized representative may be required and the process through which it will be obtained.
  - Describe any unusual consent-related issues pertaining to this study.

[1] For additional information, refer to the U.S. Department of Health and Human Services' Office of Human Research Protections website at http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm

- **Risk and Intent to Benefit**
  - Describe the most prominent risks involved in study participation (physical, psychological, legal, social, economic, etc.) and the measures that will be taken to minimize and/or manage them.
  - Describe the potential benefits to individual study subjects and to society.
  - Describe the intent to benefit for those subjects unable to provide their own consent, if applicable.
- **Description of the Safety Monitoring Procedures To Be Used in the Protocol**
  - Define adverse events for this study.
  - Describe the process for reporting serious and unexpected adverse events.
- **Proposed Plan for Study Subject Confidentiality**
  - Describe the strategy for protecting the privacy and confidentiality of research subjects and study data/records.
  - Describe any expected circumstances under which complete confidentiality cannot be guaranteed.
- **Status of Food and Drug Administration (FDA) Submission (IND, IDE, NDA, PMA, 510K, etc.), if applicable**
  - If the clinical study involves the use of a drug, biologic, or device not yet approved for marketing by the FDA or not yet approved for the indication addressed in the study, state the status of the applicable FDA submission.
  - Identify who will serve as the clinical trial sponsor.
  - Indicate whether the institution has previous experience working with the FDA in developing and conducting clinical trials and provide the location of the regulatory staff who will oversee FDA submissions. Additionally, insure that there is a provision for FDA-required clinical monitoring of the clinical trial.
- **Local Institutional Review Board (IRB) Requirements**
  - Provide the contact information (name, title, address, email, and phone number) for the IRB point of contact.
  - If local IRB review and approval has taken place, provide a copy of the IRB's approval documentation (please appended this to the summary).

b. Human Data and/or Biological Substances

- Provide a detailed plan for use of human data (exclusive of human subjects above) in the proposed research. Human data includes privileged or protected health information such as graphic, written or recorded information derived from individually identifiable human subjects.

- Provide a detailed description of human biological specimens (e.g., cells, tissues, blood) or the sources of existing biological specimens or cell lines (e.g., commercially purchased cell lines) to be used in this research.
- Provide the contact information for the IRB point of contact.
- If the review is complete, provide a letter from the local IRB stating that the review has taken place and is approved.

ATTACHMENT 4

GUIDELINES FOR SOW DEVELOPMENT

The Statement of Work (SOW) is a concise restatement of the research proposal that outlines and establishes the Principal Investigator's (PI's) performance expectations and timeline for which the US Army Medical Research and Materiel Command will provide financial support. Although some allowance is made for problems encountered and uncertainties that are part of research, the PI is expected to meet the provisions and milestones in the SOW.

The SOW should be a series of relatively short statements that outline step-by-step how each of the major goals or objectives of the proposed research/services will be accomplished. The SOW should:

- Describe the work to be accomplished as tasks (tasks may relate to specific aims).
- Identify the timeline and milestones for the work over the period of the proposed effort and list in order of progression over time.
- Identify methods.
- Indicate the number of research subjects (animal species or human) and/or anatomical samples projected or required for each task.
- Indicate time required for human use approval and FDA submission of applicable documents (i.e., IND and IDE).
- Identify outcomes, products, and deliverables for each phase of the project.
- Include the following information for each study site/subcontract site (collaborative site and consultant) that will be actively participating in the study:
    - Institution name
    - Institution address
    - Co-PI name
    - Animal or human use at this site

Sample Statement of Work

Development of a Bovine Milk Immunoglobulin Supplement that Prevents Traveler's Diarrhea by Blocking Pathogen Adherence

Study Site Information

Naval Medical Laboratory
PI: CAPT John Doe
Enteric Disease Section
1800 Street Address
Any Town, US 12345
(Animal Use Site: Aotus monkey challenge model development and passive protection studies).

Subcontract:
Ajax Antibody Industries
Co-PI: Dr. Albert Mills
Chief Scientific Officer
46 Street Address
Another Town, US 23456
(Animal Use Site: Bovine Immunization).

Subcontract:
Number One University
Co-PI: Dr. Robert Ado
Immunotherapy Research Center
78 One Way Street
Town, US 34567
(Human Use Site: Adult volunteer clinical trial of challenge model and development protection studies).

Project Tasks

Task 1. Process development, manufacturing scale-up, and characterization of antigens for bovine immunization (Months 1-12):

a. Develop expression technology and processes for purification of Fimbriae X and tip Adhesin X (Mos. 1-4). Miller, Ajax Antibody Industries
b. Develop ELISA assays for measurement of specific antibodies against each of the two antigens (Mos. 1-12). Doe, Naval Medical Laboratory
c. Submit animal use documents for approvals (Mos. 1-4). Doe, Naval Medical Laboratory
d. Submit human use documents for IRB approvals (Mos. 6-12). Doe, Naval Medical Laboratory

Task 2. Manufacture of antigens for bovine immunization, purification of high-titer bovine milk immunoglobulin products (BIgG), powder formulation and product characterization (Mos. 4-14):

a. Manufacture Fimbriae X and Adhesin X for bovine immunization (Mos. 5-6). Miller, Ajax Antibody Industries

b. cGMP production and characterization of high-titer BIgG against Fimbriae X and Adhesin X (Mos. 6-12). Miller, Ajax Antibody Industries

c. IND filing of Fimbriae X product data packages (Mos. 13-14). Miller, Ajax Antibody Industries

Task 3. Validation of nonhuman primate (Aotus nancymae) challenge model for Fimbriae X-*Escherichia coli* (ETEC) strain P98407 (Mos. 9-18):

a. Identify virulent X-ETEC strain and define challenge parameters (maximum 13 monkeys) (Mos. 9-12). Doe, Naval Medical Laboratory

b. Define challenge doses of down-selected X-ETEC strain that elicit ca. 80% diarrhea attack rates (maximum 15 monkeys) (Mos. 13-17). Doe, Naval Medical Laboratory

c. Produce cGMP stock and production seed of X-ETEC strain (Month 18). Miller, Ajax Antibody Industries

Task 4. Determine efficacy of anti-X fimbrial and anti-X adhesin BIgG by passive protection studies in Aotus nancymae monkey model (Mos. 17-28):

a. 3-arm (X fimbrial BIgG, X adhesin BIgG, placebo) passive protection against homologous ETEC (X-ETEC) (maximum 30 monkeys) (Mos. 17-28). Doe, Naval Medical Laboratory

Task 5. Validation of X-ETEC virulence in adult volunteer challenge model (Mos. 20-22):

a. Validate virulence of X-ETEC strain P98407 (Mos. 20-22) (maximum 5 volunteers). Ado, Number One University

Task 6. Determine efficacy of X fimbriae and X adhesin BIgG by passive protection studies in adult volunteers following homologous (X-ETEC) challenge (Mos. 23-36):

a. Three-arm (X fimbrial BIgG, X adhesin BIgG, control) passive protection against homologous ETEC (X-ETEC) (maximum 30 subjects) (Mos. 23-31). Ado, Number One University

b. IND filing of X fimbrial BIgG, X adhesin BIgG (Mos. 32-36). Doe, Naval Medical Laboratory