General Application Instructions

Fiscal Year 2012

Defense Health Program

Department of Defense

Congressionally Directed Medical Research Programs

Table of Contents

I. HELPFUL INFORMATION 2

A. Tips for Success 2

B. Funding Opportunities 2

C. Receiving Emails from the CDMRP, CDMRP eReceipt System, and Grants.gov 2

D. Agency Contacts 2

II. SUBMISSION INFORMATION 3

A. Submission Dates and Times 3

B. Content and Form of Pre-Application Submission 4

C. Content and Form of Application Submission 5

APPENDIX 1 Eligibility Information 19

APPENDIX 2 Formatting Guidelines 20

APPENDIX 3 GRANTS.GOV Requirements 21

APPENDIX 4 Administrative Information 23

APPENDIX 5 Regulatory Requirements 26

APPENDIX 6 Acronym List 32

APPENDIX 7 DOD/VA mTBI Definition 34

I. HELPFUL INFORMATION

A. Tips for Success

This symbol marks helpful hints throughout this document.

This symbol refers to the Program Announcement/Funding Opportunity for specific instructions.

B. Funding Opportunities

To view all funding opportunities offered by the Congressionally Directed Medical Research Programs (CDMRP), perform a Grants.gov (http://www.grants.gov/) search using the Catalog of Federal Domestic Assistance (CFDA) Number 12.420. Additional information may be found on the CDMRP website at http://cdmrp.army.mil/funding/prgdefault and on the CDMRP eReceipt System website at https://cdmrp.org/Program_Announcements_and_Forms/. To receive email notifications when CDMRP funding opportunities are released, submit a request via email to help@cdmrp.org. Email notifications of funding opportunities are sent as a courtesy and should not be used as a sole source of notification; applicants should monitor Grants.gov for official postings of funding opportunities.

C. Receiving Emails from the CDMRP, CDMRP eReceipt System, and Grants.gov

To help ensure that all email correspondence is delivered correctly and is not treated as spam by email programs, please keep your email address up to date in the CDMRP eReceipt System and Grants.gov and place the following domains into the safelist/whitelist: army.mil, amedd.army.mil, us.army.mil, cdmrp.org, and grants.gov.

D. Agency Contacts

1. **CDMRP Help Desk:** Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through the CDMRP eReceipt System should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern time. Response times may vary depending upon the volume of inquiries. Be advised that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

   Phone: 1-301-682-5507

   Email: help@cdmrp.org

2. **Grants.gov Contact Center:** Questions related to application submission through the Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. Federal holidays).

   Phone: 1-800-518-4726

   Email: support@grants.gov

II. SUBMISSION INFORMATION

Submission is a multi-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative rejection of the duplicative application.

The Principal Investigators (PIs) and organizations identified in the application submitted through Grants.gov should be the same as those identified in the pre-application.

For specific instructions regarding changes to the PI or organization, refer to the Program Announcement/Funding Opportunity.

On occasion, the CDMRP may update or change the application package in Grants.gov. The applicant must use the latest version of the application package; applications submitted with a different version of the application package may not be accepted by Grants.gov. ***Sign up in Grants.gov (http://www.grants.gov/) for "Send me change notification emails"*** by following the link on the Synopsis page for the specific Program Announcement/Funding Opportunity.

Submission of applications from U.S. Federal agencies has additional submission requirements. See Section 4: Research & Related Budget, Budget Instructions, Section K: Budget Justification. Any applicant planning to use a third party entity to administer award funding should submit the application through that entity.

A. Submission Dates and Times

All pre-application and application components must be submitted by the deadlines identified in the Program Announcement/Funding Opportunity. Material submitted after the deadlines, unless specifically requested by the Government, will not be forwarded for processing. Failure to meet any one of the deadlines will result in application rejection.

Start the submission process early, at least 72 hours before the application submission deadline. Both the CDMRP eReceipt System and Grants.gov have a number of required steps that must be completed before submissions will be accepted. Make sure to allow adequate time for completion of all pre-application and application steps by their respective deadlines.

Ensure that the organization's correct Data Universal Numbering System (DUNS) number and valid, non-expired Central Contractor Registry (CCR) number are entered accurately prior to completing the application process. In addition, each applicant organization must have a valid Commercial and Government Entity (CAGE) Code. See Appendix 3 for additional information.

B. Content and Form of Pre-Application Submission

All pre-application components must be submitted through the CDMRP eReceipt System (https://cdmrp.org/) by the deadline specified in the Program Announcement/ Funding Opportunity; otherwise, the pre-application will remain in draft status and will not be accepted.

The pre-application consists of the following components, which are organized in the CDMRP eReceipt System by separate tabs.

For specific instructions regarding content of the pre-application submission components, refer to the Program Announcement/Funding Opportunity.

Application Information – Tab 1: Enter the application information as described in the CDMRP eReceipt System before continuing the pre-application.

Application Contacts – Tab 2: Enter contact information for the PI and the organization's Business Official responsible for sponsored program administration (or equivalent). This is the individual listed as the "person to be contacted on matters involving this application" in Block 5 of the Grants.gov SF424 form. The Business Official's contact information is required or the pre-application will not be accepted; however, the CDMRP does not require approval of the pre-application by the PI's organization.

Collaborators and Conflicts of Interest (COIs) – Tab 3: To enable the CDMRP to avoid COIs during the screening and review processes, list the names of all scientific participants in the proposed research project, including co-investigators, mentors, collaborators, consultants, and subawardees. Add all individuals outside of the application who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship) and choose "COI" from the drop-down list.

No member of the FY12 Integration Panel (IP) for the program to which an application is submitted may be named as being involved in the research proposed or found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document. A list of the FY12 IP members for any CDMRP program may be found on that program's page within the CDMRP website (http://cdmrp.army.mil/).

To preserve the integrity of its peer and programmatic review processes, the CDMRP discourages the inclusion of any employee of its review contractors in applications for funding. For FY12, the peer review contractors are SRA International, Inc. and the American Institute of Biological Sciences (AIBS). The programmatic review contractor is Science Applications International Corporation (SAIC). Applications including personnel from any of these companies will be administratively withdrawn unless plans to mitigate conflicts of interest are deemed appropriate by the Government.

For questions related to this topic, contact the CDMRP Help Desk at help@cdmrp.org or 301-682-5507.

Required Files – Tab 4: Upload all documents as individual PDF files. Documents should conform to the formatting guidelines outlined in Appendix 2.

At this time, eReceipt is unable to read files made with Adobe Acrobat PDFMaker 9.0.

Submit Pre-Application – Tab 5: Enter password in the space provided next to "Enter Your Password Here" and press the "Submit" button. Press the "Confirm Submission" button to complete the pre-application submission.

Confirm that the pre-application has been submitted by verifying that the status listed in the CDMRP eReceipt System has changed from "DRAFT" to "SUBMITTED." ***Applicants with pre-applications in draft status after the pre-application submission deadline are ineligible to submit an application.***

Other Documents Tab: This tab is not applicable unless other documents are specifically requested by the CDMRP in the Program Announcement/Funding Opportunity.

C. Content and Form of Application Submission

Each application submission must include the completed Grants.gov application package of forms associated with the specific Program Announcement/Funding Opportunity in Grants.gov (http://www.grants.gov/). Refer to Appendix 3 for additional information on Grants.gov requirements.

The CDMRP cannot make allowances/exceptions to its policies for submission problems encountered using system-to-system interfaces with Grants.gov.

Submit applications at least 72 hours before the application submission deadline to allow time for Grants.gov validation of the application and, if necessary, resubmission as a "Changed/Corrected Application" prior to the deadline.

A compatible version of Adobe Reader must be used to view, complete, and submit the Grants.gov application package. ***Grants.gov will reject an application package that is opened at any point in time with an incompatible version of Adobe Reader.*** If multiple individuals are working on the same application package, all must use a compatible version of Adobe Reader. If an application is rejected due to use of an inappropriate Adobe Reader version, a new application package must be downloaded, completed, and submitted using a supported version of Adobe Reader.

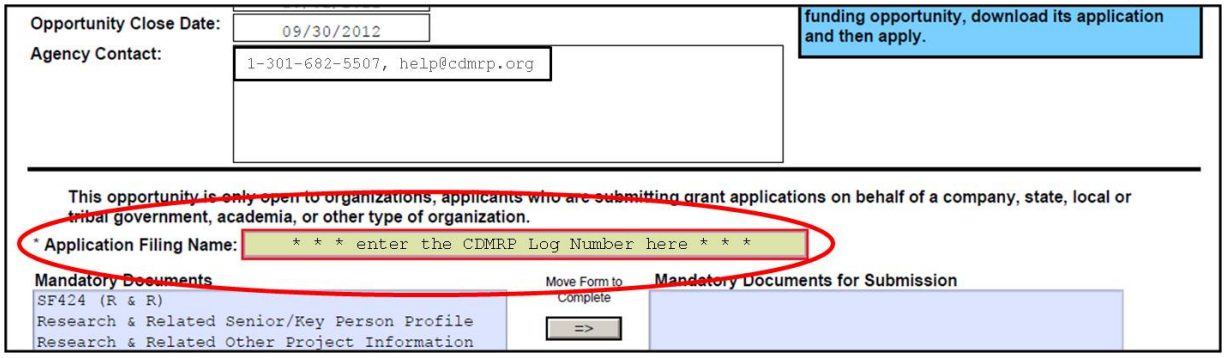
Visit the following website to verify that the version of Adobe Reader being used is compatible with Grants.gov: http://www.grants.gov/applicants/AdobeVersioningTestOnly.jsp, or download a no-cost compatible version at http://www.grants.gov/help/download_software.jsp.

CDMRP Log Number

During the pre-application process, each submission will be assigned a unique log number by the CDMRP eReceipt System. The corresponding Grants.gov application package must be submitted using this unique CDMRP log number. Enter the CDMRP log number in one of two ways:

- **Manual Entry:** Fill in the **Application Filing Name** on the first screen of the Grant Application Package (Figure 1) using only the **CDMRP log number** (e.g., PC12####, BC12####, OC12####, NF12####, etc.) assigned during the pre-application process.

Figure 1. Application Filing Name



- **System-to-System Entry:** If a system-to-system interface with Grants.gov is being used, then enter the CDMRP log number acquired during the pre-application process into the **Submission Title** field.

The application consists of the following components:

Each attachment to the Grants.gov application forms must be an individual PDF file in accordance with the formatting guidelines listed in Appendix 2.

1. SF 424 (R&R), Application for Federal Assistance Form

All appropriate information must be entered into this form to allow for auto-population of subsequent forms in this application package. See below for clarification to general instructions:

- **Block 1 – Type of Submission.** For original submissions, select the "Application" box. For changes that must be made after the original submission, the complete application package must be resubmitted with the "Changed/Corrected Application" box selected.
- **Block 2 – Date Submitted.** Enter the date the application is submitted.
  - **Applicant Identifier.** Enter the submitting organization's Control Number, if applicable. This information can be obtained from the organization's Office of Sponsored Research or business unit responsible for contracting. If there is no Organization Control Number, leave this field blank.
- **Block 3 – Date Received by State.** Not applicable.

- **State Application Identifier.** Not applicable.
- **Block 4 – a. Federal Identifier Box.** This box will be populated by Grants.gov for an original application. For changed/corrected applications, enter the Grants.gov tracking number (the Federal Identifier Number assigned to the original application).
- **Block 4 – b. Agency Routing Identifier.** Not applicable.
- **Block 5 – Applicant Information.** Enter the information for the applicant organization. The "Person to be contacted on matters involving this application" is the Business Official.
- **Block 6 – Employer Identification.** Enter the Employer Identification Number (EIN) or Tax Identification Number (TIN) as assigned by the Internal Revenue Service. If applying from an organization outside the United States, enter 44-4444444.
- **Block 7 – Type of Applicant.** Enter the information for the applicant organization.
- **Block 8 – Type of Application.** Select "New" for all submissions.
- **Block 9 – Name of Federal Agency.** Populated by Grants.gov.
- **Block 10** – **Catalog of Federal Domestic Assistance Number.** Populated by Grants.gov.
- **Block 11 – Descriptive Title of Applicant's Project.** Enter the same project title as used for the pre-application.
- **Block 12 – Proposed Project.** Enter the estimated start date for the project. The actual start date will be determined during negotiations if the application is recommended for funding.
- **Block 13 – Congressional District of Applicant.** If the applicant organization is outside the United States, enter 00-000.
- **Block 14 – Project Director/Principal Investigator Contact Information.** Enter information for the individual PI responsible for the overall scientific and technical direction of the application. If outside the United States, select the appropriate country from the drop-down menu.
- **Block 15 – Estimated Project Funding.** Enter the total funds (direct + indirect costs) requested for the entire performance period of the project. These figures should match those provided in the Research & Related Budget.
- **Block 16 – Is Application Subject to Review by State Executive Order 12372 Process?** Select option "b. NO, program is not covered by E.O.12372."
- **Block 17 – Complete Certification.** Select the "I agree" box to provide the required certifications and assurances**.**
- **Block 18 – SFLLL or Other Explanatory Documentation.** If applicable, complete and attach Standard Form LLL to disclose lobbying activities pursuant to Title 31 United States Code Section 1352 (31 USC) 1352.
- **Block 19 – Authorized Representative.** Enter the contact information for the applicant organization's authorized representative. The "Signature of Authorized Representative" is

not an actual signature and is automatically completed upon submission of the electronic application package.

- **Block 20 – Pre-Application.** Not applicable.

2. Attachments Form

For specific instructions regarding content and page limits of the Project Narrative, Supporting Documentation, and all other attachments to this Grants.gov form, refer to the Program Announcement/Funding Opportunity.

All documents that require signatures must be signed. Both electronic and hand signatures will be accepted.

The following must be included as attachments to this form:

Attachment 1: Project Narrative: Named "ProjectNarrative.pdf." The Project Narrative is the main body of the application. The page limit of the Project Narrative applies to the text and any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, and cartoons needed to support the proposed study.

Attachment 2: Supporting Documentation: Combine and attach as a **single PDF file named "Support.pdf."** Include only supporting documentation as indicated in the Program Announcement/Funding Opportunity. Submitting material that was not requested may be viewed as an attempt to gain an unfair competitive advantage, and such material will be removed. ***The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, or cartoons. These items should be included in the Project Narrative. Any additional material viewed as an extension of the Project Narrative will result in administrative rejection of the application.***

All applications are provided a fair and thorough review. Letters of support not requested in the Program Announcement/Funding Opportunity, such as those from members of Congress, do not impact application review or funding decisions.

For a list and descriptions of required supporting documents, refer to the Program Announcement/Funding Opportunity.

Attachment 3: Technical Abstract: Named "TechAbs.pdf." Abstracts of all funded research projects will be posted on the CDMRP website at http://cdmrp.army.mil. Proprietary or confidential information should ***not*** be included. ***Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.***

Attachment 4: Lay Abstract: Named "LayAbs.pdf." Abstracts of all funded research projects will be posted on the CDMRP website at http://cdmrp.army.mil. Proprietary or confidential information should ***not*** be included. ***Use only characters available on a standard***

QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

Attachment 5: Statement of Work (SOW): Named "SOW.pdf." The SOW is an outline of specific aims defined within the proposed research project that establishes the PI's performance expectations and timeline during the performance period of the award.

The SOW should include a list of major tasks that support the proposed specific aims, followed by a series of subtasks outlined step-by-step as they relate to the major tasks and milestones within the period of performance. The SOW should describe only the work for which funding is being requested by this application and, as applicable, the SOW should also:

- Include the following information for each study site/subaward site: organization; organization address; investigator(s), collaborator(s), consultant(s); animal or human use to be conducted at the site; and key personnel responsible for each major task and each subtask to be performed at the site.
- Indicate the number (and type, if applicable) of research subjects (animal or human) and/or anatomical samples projected or required for each task. As applicable, estimated times to complete each task should include time for local and Department of Defense (DoD) regulatory review and approval, as shown below. Refer to Appendix 5 for additional information regarding regulatory review.
    - For studies involving human subjects, allow at least 2 to 3 months for regulatory review and approval processes to include local Institutional Review Board (IRB) and DoD Human Research Protection Office (HRPO).
    - For animal studies, allow 2 to 3 months for regulatory review and approval processes to include local Institutional Animal Care and Use Committee (IACUC) and DoD Animal Care and Use Review Office (ACURO).
- Identify methods.
- For studies with prospective accrual of human subjects, indicate quarterly enrollment targets.
- Identify cell line(s) and commercial or organizational source(s) to be used. If human anatomical substances (including cell lines) will be used, specify whether or not identifiable information is accessible to the research team by any means.
- If applicable, indicate time required for submission and/or approval of documents (e.g., Investigational New Drug [IND] and Investigational Device Exemption [IDE]) to the U.S. Food and Drug Administration or appropriate government agency.

For any additional instructions regarding the SOW, refer to the Program Announcement/Funding Opportunity.

SOW format: There is no limit to the number of specific aims, tasks, or subtasks that are described within the SOW page limit.

Task 1. Brief overview description of this task (timeframe, e.g., months 1-18):
1a. Description of subtask 1a (timeframe, e.g., months 1-4).
1b. Description of subtask 1b (timeframe, e.g., months 6-12).
1c. Description of subtask 1c (timeframe, e.g., months 1-18).

Task 2. Brief overview description of this task (timeframe, e.g., months 4-36):
2a. Description of subtask 2a (timeframe, e.g., months 4-12).
2b. Description of subtask 2b (timeframe, e.g., months 13-25).
2c. Description of subtask 2c (timeframe, e.g., months 25-30).
2d. Description of subtask 2d (timeframe, e.g., months 25-36).

The Government reserves the right to request a revised SOW format and/or additional information.

Attachments 6-15: Additional Documents (as applicable): Attach each as a separate PDF file, named as indicated in the Program Announcement/Funding Opportunity (e.g., "Impact.pdf," "Innovation.pdf," "Training.pdf," "Transition.pdf," etc.).

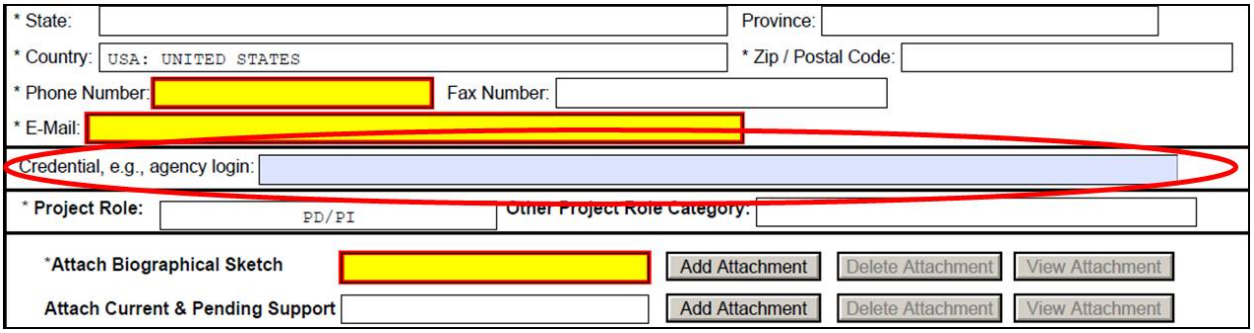
For specific instructions regarding content, titles, and page limits for the Additional Documents, refer to the Program Announcement/Funding Opportunity.

3. Research & Related Senior/Key Person Profile (Expanded)

Include the requested information for each person who will contribute significantly to the proposed research project.

In the **"**PROFILE – Project Director/Principal Investigator" section, enter the PI's User Name provided from the CDMRP eReceipt System into the data field labeled "Credential, e.g., agency login" (Figure 2).

Figure 2. Credential, e.g., agency login.



Biographical Sketch Suggested Format: The suggested biographical sketch format is available via a Microsoft Word document in the CDMRP eReceipt System on the "Program Announcement and Forms" web page (https://cdmrp.org/Program_Announcements_and_

Forms/). Use of this document is not mandatory. Each biographical sketch must be in PDF format prior to attachment.

a. **PI Biographical Sketch:** This file must be titled "Biosketch_LastName.pdf," where "LastName" is the last name of the PI.

b. **PI Current/Pending Support:** This file must be titled "Support_LastName.pdf," where "LastName" is the last name of the PI.

   For all existing and pending research support, include the title, time commitments, supporting agency, name and address of the funding agency's procuring Contracting/Grants Officer, performance period, level of funding, brief description of the project's goals, and list of the specific aims. If applicable, identify where the proposed project overlaps with other existing and pending research projects. Clearly state if there is no overlap.

   If there is no existing or pending support, enter "None." An updated existing and pending support document will be required during award negotiations.

c. **Key Personnel Biographical Sketches:** Each file must be titled "Biosketch_LastName.pdf," where "LastName" is the last name of the respective individual.

d. **Key Personnel Current/Pending Support:** Each file must be titled "Support_LastName.pdf," where "LastName" is the last name of the respective individual. Refer to content requirements under "PI Current/Pending Support" listed above.

4. Research & Related Budget

An estimate of the total proposed research project cost, with a breakdown of all cost categories for each year, must accompany each application. ***Include a sufficiently detailed budget and budget justification*** so that the Government can determine the proposed costs to be allowable, allocable, and reasonable for the proposed research. The budget justification for the entire period of performance must be uploaded to the Research & Related Budget after completion of the budget for Period 1. At the time of application submission to Grants.gov, the Authorized Organizational Representative is certifying to the best of his/her knowledge that all costs are current, accurate, and complete. Use the form for the Research & Related Budget that is available for download on the Grant Application Package page for the Program Announcement/Funding Opportunity in Grants.gov.

For limits on funding and period of performance, refer to the Program Announcement/Funding Opportunity.

Budget Regulations and Restrictions: The following must be utilized in developing the budget:

- **Maximum Obligation:** The U.S. Army Medical Research and Materiel Command (USAMRMC) does not modify awards to provide additional funds for such purposes as reimbursement for unrecovered indirect/facilities and administrative costs resulting from the establishment of final negotiated rates or for increases in salaries, fringe benefits, and other costs.
- **Administrative and Cost Principles:** Applicants are required to comply with the following, as applicable.
  - Federal Acquisition Regulation (FAR) Part 31
  - Defense FAR Supplement Part 231
  - Department of Defense Grant and Agreement Regulations 3210.6-R
  - Title 2 of the Code of Federal Regulations Part 220 (2 CFR 220), "Cost Principles for Educational Institutions (OMB Circular A-21)"
  - 2 CFR 225, "Cost Principles for State, Local, and Indian Tribal Governments (OMB Circular A-87)"
  - OMB Circular A-102, "Grants and Cooperative Agreements with State and Local Governments"
  - 2 CFR 215, "Uniform Administrative Requirements for Grants and Agreements with Institutions of Higher Education, Hospitals, and Other Non-Profit Organizations (OMB Circular A-110)"
  - 2 CFR, 230, "Cost Principles for Non-Profit Organizations (OMB Circular A-122)" [For those non-profit organizations specifically excluded from the provisions of OMB Circular A-122, FAR 48 CFR Subpart 31.2 shall apply.]
  - OMB Circular A-133, "Audits of States, Local Governments, and Non-Profit Organizations"
- **Cost of Preparing Applications:** The cost of preparing applications in response to a CDMRP Program Announcement/Funding Opportunity is not considered an allowable direct charge to any resultant contract, grant, or cooperative agreement. However, the cost of preparing applications may be an allowable expense to the indirect/facilities and administrative cost as specified in the organization's applicable cost principles.
- **Currency:** All costs must be entered in U.S. dollars. Recipients performing research outside of the United States should include the cost in local currency, the rate used for converting to U.S. dollars, and justification/basis for the conversion rate used.

Submit a detailed budget and justification that covers the entire period of performance (not just the first year). The Government reserves the right to request a revised budget and budget justification and/or additional information.

Budget Instructions: Complete the Research & Related Budget following the instructions below. Begin by entering the organizational Data Universal Numbering System (DUNS) number, Budget Type, Name of Organization, and anticipated start and end dates. ***It is very important that the DUNS number be entered accurately.***

Section A: Senior/Key Person

- **Prefix; First, Middle and Last Name; and Suffix:** Beginning with the PI, list all senior/key persons from the applicant organization who will be involved in the proposed research project, whether or not salaries are requested. Include all investigators, research associates, etc. If applicable, all investigators outside the applicant organization should be included on the R & R Subaward Budget Attachment(s) Form. Consultant costs should be listed under section F.3.
- **Project Role:** Identify the role of each senior/key person listed. Describe his/her specific functions in the budget justification.
- **Base Salary:** Enter the current annual base salary (based on a full-time appointment) for each individual listed for the proposed research project. Establish labor costs using current labor rates or salaries. Labor rates or salaries may not be increased as a result of receiving an award. Identify and explain in the budget justification any proposed adjustments to rates or salaries. Any proposed increases in rates or salaries over the period of the award must be consistent with the applicable cost principles and organization's estimating procedures.
- **Calendar, Academic, and Summer Months:** For each senior/key person, including unpaid personnel, list the number of months to be devoted to the proposed research project in the appropriate box.
- **Requested Salary:** Enter the amount of salary requested for this budget period.
- **Fringe Benefits:** Enter the fringe benefits requested for each individual in accordance with organizational guidelines. If the application is recommended for funding, the organization will be required to provide documentation to support the fringe benefits (e.g., the current Department of Health and Human Services [DHHS] Rate Agreement or other policy document).
- **Funds Requested:** Enter the total funds requested for each senior/key person listed for the proposed research project.

Section B: Other Personnel:

- **Number of Personnel:** For each project role category indicate the number of personnel for the proposed research project, including unpaid personnel.
- **Project Role:** Identify each project role category. Within the budget justification, describe the specific functions of the personnel in each project role.
- **Calendar, Academic, and Summer Months:** For each project role category, list the number of months to be devoted to the proposed research project in the appropriate box.
- **Requested Salary:** Enter the amount of salary requested for this budget period.
- **Fringe Benefits:** Enter the fringe benefits requested for each project role category in accordance with organizational guidelines. If the application is recommended for funding, the organization will be required to provide documentation to support the

fringe benefits (e.g., the current Department of Health and Human Services [DHHS] Rate Agreement or other policy document).

- **Funds Requested:** Enter the total funds requested for each project role category listed for the proposed research project.

Section C: Equipment Description: Equipment is any article of non-expendable tangible property to be charged directly to the award and having a useful life of more than 1 year and an acquisition cost of $5,000 or more per unit (unless the applicant organization's policy has established a limit lower than $5,000). Applicant organizations are encouraged to provide all equipment necessary to conduct the proposed research project. If equipment is requested, provide a detailed list showing the cost of each item. The budget justification for any requested equipment must describe, as applicable:

- Special test equipment to be fabricated for specific research purposes and its cost.
- Standard equipment to be acquired and modified to meet specific requirements, including acquisition and modification costs; list separately.
- 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 recipient with recipient funds, would be capitalized for Federal income tax purposes.

In addition, requests for equipment must include at least one of the following:

- Vendor Quote: Provide a copy of the successful vendor's quote. Any equipment purchase should be made in accordance with the recipient's approved purchasing system.
- Historical Cost: Identify the vendor, date of purchase, and whether or not the cost represented the lowest bid. Include reason(s) for not soliciting current quotes.
- Estimate: Include a rationale for the estimate and reasons for not soliciting current quotes.

Section D: Travel: Travel costs may include:

- Costs to attend one or more scientific/technical meetings per year: Costs should not exceed the amount specified in the Program Announcement/Funding Opportunity. Include the meeting name, purpose, location, and date, if known, in the budget justification. International travel is permitted but must be well justified, and costs may not exceed the allowable amount; potential restrictions will be specified in any resulting award.
- Costs for travel associated with the execution of the proposed work (if applicable): Reasonable costs for travel between collaborating organizations should be included and are not subject to the yearly cost limitation on travel to scientific/technical meetings. International travel is permitted but must be well justified; potential restrictions will be specified in any resulting award.
- Costs to attend CDMRP-required meetings (if applicable): Costs should not exceed the amount specified in the Program Announcement/Funding Opportunity, if

applicable. Include the meeting name if identified in the Program Announcement/ Funding Opportunity (e.g., Era of Hope, IMPaCT, and Military Health Research Forum) and a statement in the budget justification confirming that the PI will attend the CDMRP-required meeting. These travel costs are in addition to those allowed for annual scientific/technical meetings.

Section E: Participant/Trainee Support Costs: Enter the funds requested for tuition/fees, health insurance, stipends, travel, subsistence, and other costs.

Section F: Other Direct Costs

1. **Materials and Supplies:** The budget justification for supporting material and supply (consumable) costs should include a general description of expendable material and supplies for each year. For individual or total materials and supplies costing $5,000 or more per year, provide descriptions, quantities, and unit prices. If animals are to be purchased, state the species, strain (if applicable), number to be used, cost per animal and total costs, proposed vendor, and a copy of the animal per diem cost/rate agreement. If human cell lines are to be purchased, state the source, cost, and description.
2. **Publication Costs:** Estimate the costs of publishing and reporting research results, including direct charges for clerical preparation, illustrations, reprints, and distribution.
3. **Consultant Services:** Regardless of whether funds are requested, include in the budget justification the names and organizational affiliations of all consultants, and include the daily consultant fee, travel expenses, nature of the consulting effort, and why consultants are required for the proposed research project.
4. **ADP/Computer Services:** Include the cost of computer services, including computer-based retrieval of scientific, technical, and education information. Include in the budget justification the provider's computer service rates.
5. **Subaward/Consortium/Contractual Costs:** Include the total funds requested for (1) all subaward/consortium organization(s) proposed for the research project and (2) any other contractual costs proposed for the research project. This amount should be supported in the subaward/consortium/contractual costs provided in the R & R Subaward Budget Attachment(s) Form.

All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.

6. **Equipment or Facility Rental/User Fees:** List proposed equipment or facility rental/user fees. Include appropriate information (hours and rates) in the budget justification.
7. **Alterations and Renovations:** Alteration and renovation (A&R) costs can be requested if the costs are essential to accomplish the objectives of the research project and are a minor portion of the overall budget. A description of the existing facility and detailed description of the requested changes, along with a cost estimate, must be

included in the budget justification. Costs for the construction of facilities are not allowable.

8. **Other Expenses:** Itemize other anticipated direct costs such as communication costs and organizationally provided services. These items should be described in detail and clearly justified. Unusual or expensive items should be fully explained and justified in the budget justification. Organizationally provided services should be supported by the organization's current cost/rate schedule.

   Computers and software are considered to be general office supplies and are not normally allowable direct cost charges unless the computer/software is essential and unique to the proposed research project. If a computer/software purchase is requested, include the following in the budget justification:

   - Detailed explanation for why purchase of computer/software is required to complete the proposed research project.
   - Statement verifying that the requested computer/software is not currently available for use by the PI.
   - Statement assuring that the requested computer/software will be purchased in accordance with applicable cost principles.

   Include itemized research-related subject costs for the proposed research project. These costs are strictly limited to expenses specifically associated with the proposed research project.

Section G: Direct Costs: Include the total direct costs (A-F).

Section H: Indirect Costs: The indirect costs category may include Facilities and Administrative (F&A) costs, overhead, General and Administrative (G&A), and other. The most recent Federal agency approved rate(s) should be applied. If the rate(s) has been approved by other than a Federal agency, indicate the source of the approval.

Provide details of the direct cost base (modified total direct costs, salary and wage, or other). Identify any costs that have been excluded from the base (in accordance with the approved rate agreement). Also indicate if the rate(s) is an on- or off-site rate(s). If more than one rate is applicable, provide a breakdown of the calculation.

Provide documentation to support the indirect cost rate (e.g., the current DHHS Rate Agreement or other policy document) via the CDMRP eReceipt System (https://cdmrp.org).

If a negotiated approved rate(s) does not exist, provide sufficient detail for a proposed rate (adhering to the applicable cost principles) in the budget justification. Organizations can also visit the Department of Health and Human Services (http://rates.psc.gov/fms/dca/negotiations.html), the Office of Naval Research (http://www.onr.navy.mil/Contracts-Grants/manage-grant/indirect-cost-proposal.aspx), and the Defense Contract Audit Agency (http://www.dcaa.mil/) for additional information on indirect rates.

Section I: Total Direct and Indirect Costs: Include total costs for the proposed research project.

Section J: Fee: Charging a fee or profit to an assistance agreement, either by the recipient, subrecipient, or subcontractor, is prohibited.

Section K: Budget Justification: Provide a clear budget justification for each item in the budget over the entire period of performance and attach as a single PDF file to section K of the Research & Related Budget.

Organizations must provide sufficient detail and justification so the Government can determine that the proposed costs are allowable, allocable, and reasonable for the proposed research effort.

Federal Agency Financial Plan (if applicable): Applications from Federal agencies must include in their budget justifications a plan delineating how all funds will be obligated before their expiration for obligation, 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 through agreements with foundations, non-Federal organizations, universities, or through other means.

It should be noted, however, that it is contrary to policy to allow for any recipient to reimburse a U.S. Government entity for any costs except under very limited circumstances provided for in USAMRAA policy.

5. Project/Performance Site Location(s) Form

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. Add more sites as necessary using the "Next Site" button. If more than eight performance site locations are proposed, provide the requested information in a separate file and attach it to this form. Each additional research site requesting funds will require a subaward budget.

6. R & R Subaward Budget Attachment(s) Form (if applicable)

Complete a separate detailed Research & Related Budget including a budget justification for each subaward (subgrant or subcontract) in accordance with the instructions listed above. Title each individual subaward, "Research & Related Budget," with the name of the subawardee organization, and attach to the R & R Subaward Budget Attachment(s) Form.

All direct and indirect costs of any subaward must be included in the total direct costs of the primary award.

A description of services or materials that are to be provided under the subaward is required. Organizations must provide sufficient detail and justification so that the Government can determine

that the proposed costs are allowable, allocable, and reasonable for the proposed research effort. The following information must be provided on subawards:

- Identification of the type of subaward to be used (e.g., cost reimbursement, fixed price).
- Identification of the proposed subcontractor or subrecipient, if known, and an explanation of why and how the subcontractor or subrecipient was selected or will be selected.
- Whether the subaward will be competitive; if non-competitive, rationale to justify the absence of competition.
- The applicant's cost or price analysis for the subaward that supports the allowability, allocability, and reasonableness of the proposed cost or price.

APPENDIX 1

ELIGIBILITY INFORMATION

To protect the public interest, the Federal Government ensures the integrity of Federal programs by only conducting business with responsible recipients. The US Army Medical Research and Materiel Command (USAMRMC) utilizes the Excluded Parties List System (EPLS) to identify individuals and organizations ineligible to receive Federal awards. More information about the EPLS is available at https://www.epls.gov/. (Reference: Department of Defense Grant and Agreement Regulations [DODGAR].3210.R. Part 1125.) In addition, there is a pending Government-wide policy on the use of the Federal Awardee Performance and Integrity Information System (FAPIIS) in the award of grants and agreements that may affect agencies' processes for judging proposed recipients to be qualified to receive financial assistance awards. The policy will implement section 872 of the Duncan Hunter National Defense Authorization Act for FY2009 (P.L. 110-417). For additional background information, see the Supplemental Information section in the Office of Management and Budget's (OMB) proposal of the policy for comment, which appeared in the Federal Register on February 18, 2010 [75 FR 7319]. Until such time as the policy is finalized, Grant Officers will continue the standards in 32 CFR 22 to determine proposed recipients' qualifications for award. It is anticipated that use of FAPIIS will begin in 2013.

A. Eligible Investigators: Includes all individuals, regardless of ethnicity, nationality, or citizenship status, who are employed by, or affiliated with, an eligible organization. Investigators must meet the specific Program Announcement/Funding Opportunity requirements.

B. Eligible Organizations: The USAMRMC makes awards to national and international organizations. Eligible organizations include for-profit, non-profit, public, and private organizations, such as universities and colleges (including historically black colleges and universities, and minority institutions), hospitals, laboratories, and companies.

C. Government Agencies within the United States: Local, state, and Federal Government agencies are eligible to the extent that applications do not overlap with their fully funded intramural programs. Such agencies are required to explain how their applications do not overlap with their intramural programs.

APPENDIX 2

FORMATTING GUIDELINES

All pre-application and application documents must be legible, and should 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 in PDF.
- **Font Size:** 12 point, 10 pitch.
- **Font Type:** Times New Roman.
- **Spacing:** Single space or 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 (21.59 cm x 27.94 cm).
- **Margins:** At least 0.5 inch (1.27 cm) in all directions.
- **Print Area:** 7.5 inches x 10.0 inches (19.05 cm x 25.40 cm).
- **Color, High-Resolution, and Multimedia Objects:** Project narratives and pre-application files may include color, high-resolution, or multimedia objects (e.g., MPEG, WAV, or AVI files) embedded in the PDF files; however, these objects should not exceed 15 seconds in length and a size of 10 MB. Photographs and illustrations must be submitted in JPEG format; bit map or TIFF formats are not allowed.
- **Scanning Resolution:** 100 to 150 dots per inch.
- **Internet URLs:** URLs directing reviewers to websites containing additional information about the proposed research are not allowed in the application or its components. Inclusion of such URLs may be perceived as an attempt to gain an unfair competitive advantage. However, links to publications referenced in the application are encouraged.
- **Language:** All documents must be submitted in English, unless otherwise specified in the Program Announcement/Funding Opportunity (e.g., foreign transcripts submitted with English translations).
- **Headers and Footers:** Should not be used. Pre-existing headers and footers on required forms are allowed.
- **Page Numbering:** Should not be used.
- **Recommended Attachment Size:** Each attachment should not exceed 20 MB.

APPENDIX 3

GRANTS.GOV REQUIREMENTS

Prior to submission of an application through Grants.gov, a pre-application must be submitted to the CDMRP eReceipt System at https://cdmrp.org for all Congressionally Directed Medical Research Programs (CDMRP) Program Announcements/Funding Opportunities. This is a required step. Following pre-application submission to the CDMRP eReceipt System, applications must be submitted through the Federal Government's single entry portal, Grants.gov.

Organizations must register in Grants.gov to submit applications through the Grants.gov portal. The registration process may take several weeks, so organizations should register as soon as possible.

If business is conducted with the Federal Government on a continuing basis, it is likely that some of the actions have already been completed, e.g., obtaining a Data Universal Numbering System (DUNS) number or registration in the Central Contractor Registry (CCR). Detailed information, automated tools, and checklists are available at http://www.grants.gov/applicants/get_registered.jsp.

The following actions are required as part of the registration process:

A. Data Universal Numbering System (DUNS) Number: The applicant organization and all subrecipient organizations must have a DUNS number. A DUNS number is a unique nine-character identification number provided by the commercial company Dun & Bradstreet. If an organization does not have a DUNS number, an authorized business official of the organization can request one by calling 866-705-5711 or by registering online (http://fedgov.dnb.com/webform/displayHomePage.do). Organizations located outside of the United States can request and register for a DUNS number online via web registration.

B. Central Contractor Registry (CCR): The applicant organization must be registered with the CCR (http://www.ccr.gov) before submitting an application through Grants.gov. The CCR validates organization information and electronically shares the secure and encrypted data with Federal agencies' finance offices to facilitate paperless payments through electronic funds transfer. An organization must identify an E-Business point of contact (E-Biz POC) during the CCR registration process. ***CCR registrations have an annual expiration. Verify the status of your organization's CCR registration well in advance of the application submission deadline.*** An organization can register by calling the CCR Assistance Center at 866-606-8220 or 334-206-7828, or by registering online at www.ccr.gov. Collecting the information (Employer Identification Number [EIN] or Tax Identification Number [TIN]) can take 1-3 days. If you have the necessary information, online registration will take about 30 minutes to complete, depending upon the size and complexity of your organization. Allow a minimum of 5 business days to complete the entire CCR registration. If your organization does not have either an EIN or TIN, allow at least 2 weeks to obtain the information from the Internal Revenue Service.

As of August 9, 2011, applications will be rejected by Grants.gov if the organization's CCR registration is not current and accurate.

C. Commercial and Government Entity (CAGE) Code: The applicant organization must have a CAGE Code. The Defense Logistics Information Service in Battle Creek, Michigan, is the only

authorized source of CAGE Codes. CAGE Codes will be assigned to registrants as their CCR registration goes through the validation process. Foreign registrants in CCR must have a NATO CAGE Code (NCAGE) assigned. An NCAGE code can be obtained by contacting the National Codification Bureau of the country where the company is located or by connecting to Form AC135 (http://www.dlis.dla.mil/Forms/Form_AC135.asp).

D. Authorized Organization Representative (AOR): Each organization must have an AOR who is registered with Grants.gov. Individual Principal Investigators do not register with Grants.gov; the Authorized Organizational Representative (AOR) is required to register. An organization's E-Biz POC must authorize an AOR. An individual may serve as both the E-Biz POC and the AOR. Before submitting an application, an organization representative must register to submit on behalf of the organization at Grants.gov (http://apply07.grants.gov/apply/OrcRegister).

An AOR must first register with the Grants.gov credential provider at http://apply07.grants.gov/apply/OrcRegister to obtain a username and password. Once an AOR has completed the Grants.gov process, Grants.gov will notify the E-Biz POC for assignment of user privileges. When an E-Biz POC approves an AOR, Grants.gov will send the AOR a confirmation email.

At the time of application submission to Grants.gov, the AOR is certifying to the best of his/her knowledge that all information provided in the application is current, accurate, and complete.

APPENDIX 4

ADMINISTRATIVE INFORMATION

A. Defense Health Program Authority

The Office of the Assistant Secretary of Defense for Health Affairs [OASD(HA)] exercises authority, direction and control over Defense Health Program Research, Development, Test and Evaluation activities including certain Congressional Special Interest (CSI) appropriations. The OASD(HA) established an Interagency Support Agreement with the U.S. Army Medical Research and Materiel Command (USAMRMC) to manage the execution of these CSI appropriations. Within USAMRMC, the Congressionally Directed Medical Research Programs (CDMRP) is responsible for the day-to-day execution functions of these CSI appropriations, and performs activities such as developing solicitations for applications for funding, conducting peer and programmatic review of applications, and overall program management. Other USAMRMC organizations are responsible for award of assistance agreements or contracts, funds management, and a variety of follow-on program management, legal and regulatory review, and compliance actions.

B. Disclosure of Proprietary Information Included in an Application

Proprietary information submitted in an application may be disclosed outside the Government for the sole purpose of technical evaluation. The USAMRMC will obtain a written agreement from the evaluator that proprietary information in the application will be used for evaluation purposes only and will not be further disclosed or used. All applications may be subject to public release under the Freedom of Information Act.

C. Award Negotiations

Extramural research programs are implemented predominantly through the award of assistance agreements that are made to an organization, not to the individual Principal Investigator(s) (PI[s]). A representative from the U.S. Army Medical Research Acquisition Activity (USAMRAA) will contact the business official authorized to negotiate on behalf of the PI's organization. The award start date will be determined during the negotiation process.

Only an appointed USAMRAA Grants Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government should be inferred from discussions with any other individual. Any pre-award costs associated with a research effort are made at an organization's own risk. The incurring of pre-award costs by an organization does not impose any obligation on the Government in the absence of appropriations, if an award is not made, or if an award is made for a lesser amount than an organization expected.

D. Administrative and National Policy

The award provisions of Appendix B to Part 22 of the DODGAR 3210.6-R apply to all assistance agreements (http://www.dtic.mil/whs/directives/corres/pdf/321006r22apbp.pdf). Refer to this General Applications Instructions, Appendix 5, for further regulatory requirements.

Award recipients will also be required to complete "Certifications and Assurances for Assistance Agreements" (https://www.usamraa.army.mil/pages/regulatory/APR_2003_Certs_Assurances.pdf) prior to award.

E. Reporting Requirements for Awards

The Government requires periodic reports to be submitted to continue the research and funding through the entire period of performance. Specific reports required by the Government will be described in each award and may include: quarterly, mid-term, annual, and final research progress reports; fiscal reports; non-exempt human studies reports; and animal use reports. USAMRMC research progress reporting requirements and instructions can be found at https://mrmc-www.army.mil/index.cfm?pageid=mrmc_resources.rrpindex. Forms for fiscal and animal use reports can be found at https://www.usamraa.army.mil/index.cfm?ID=12&Type=3#Forms. The Government may request additional reports, which will be identified in the award.

F. Organization or PI Changes after Award Initiation

Unless restricted by the specific Program Announcement/Funding Opportunity, a change in organizational affiliation will be considered by the USAMRAA Grants Officer and will require the PI's original organization to agree to relinquish the award. The new organization will be required to resubmit the entire application packet to USAMRAA on behalf of the PI. The application packet must include regulatory documentation to be approved for the new organization. Unless otherwise restricted, changes in PI will be made at the discretion of the USAMRAA Grants Officer, provided that the intent of the award mechanism is met.

G. Equipment

Unless otherwise specified in the award, the title to equipment or other tangible property purchased with Government funds will vest in institutions of higher education or with non-profit organizations whose primary purpose is conducting scientific research. Normally, the title will vest in the recipient if vesting will facilitate scientific research performed by the organization for the Government. Title to equipment or other tangible property purchased by for-profit organizations will conditionally vest in the organization subject to the requirements of the DODGAR 3210.6-R, Part 34.21. However, if the award is subsequently transferred to a new organization, the Department of Defense (DoD) reserves the right to require the transfer of equipment purchased with the award funds to the Federal Government or to an eligible third party.

H. Inquiry Review

If an application is not recommended for funding, the organization or PI may submit an inquiry within 30 business days after the date on which the funding status notification email for that

application is sent. The inquiry must specifically address a factual or procedural error that is believed to have occurred during review of the application. Inquiries in response to funding recommendations should be submitted to the USAMRAA Grants Officer through the CDMRP Help Desk at help@cdmrp.org. An inquiry review panel will determine whether a factual or procedural error occurred in either peer or programmatic review and, if so, recommend corrective action where appropriate. Considering the recommendation of the inquiry review panel, a final determination will be made by the USAMRAA Grants Officer and is not subject to appeal. Questions related to the inquiry review process prior to or after submitting an inquiry should be directed to the CDMRP Help Desk at help@cdmrp.org.

I. J-1 Visa Waiver

Each organization is responsible for ensuring that the personnel associated with any application recommended for funding are 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.

J. Title to Inventions and Patents

In accordance with the Bayh-Dole Act (Title 35, United States Code, Sections 200 et seq.), the recipient and collaborators may elect to retain title to their subject inventions, but the U.S. Government shall, at a minimum, retain non-exclusive rights for the use of such inventions. Instructions in the assistance agreement concerning subject inventions must be followed.

APPENDIX 5

REGULATORY REQUIREMENTS

Principal Investigators (PIs) and applicant organizations may not use, employ, or subcontract for the use of any human participants, human anatomical substances and/or human data, or laboratory animals until applicable regulatory documents are requested, reviewed, and approved by U.S. Army Medical Research and Materiel Command (USAMRMC) to ensure that Department of Defense (DoD) regulations are met. All expectations described below are consistent with the new DoD Instruction (DoDI) 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research," as issued on November 8, 2011, and available at http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf.

Studies involving animals and non-exempt research involving human subjects (to include direct intervention/interaction, obtaining individually identifiable information, and obtaining individually identifiable anatomical substances), must be approved through a regulatory review process by the PI's local Institutional Animal Care and Use Committee (IACUC) or Institutional Review Board (IRB) and by the USAMRMC Office of Research Protections (ORP). The ORP Animal Care and Use Review Office (ACURO) is responsible for administrative review, approval, and oversight of all animal research. The ORP Human Research Protection Office (HRPO) is responsible for administrative review, approval, and oversight of research involving human subjects. ***Research involving human subjects that is anticipated to be exempt from human subjects protections regulations requires a determination from the PI's institution as well as the ORP at USAMRMC.*** A timeframe for submission of the appropriate protocols and required approvals will be established during negotiations.

Concurrent with the U.S. Army Medical Research Acquisition Activity 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.

A. Certificate of Environmental Compliance

The Certificate of Environmental Compliance will be requested prior to award negotiations. If multiple research sites/organizations are included in the application, then a Certificate of Environmental Compliance for each site will also be requested. The Certificate of Environmental Compliance can be downloaded from the CDMRP eReceipt System at https://cdmrp.org/Program_Announcements_and_Forms/.

B. Safety Program Documents

The Principal Investigator Safety Program Assurance form will be requested prior to award negotiations. If multiple research sites/organizations are included in the application, then a Safety Program Assurance form for each site will also be requested.

A Facility Safety Plan will be requested from each research site/organization funded by the award. Specific requirements for the Facility Safety Plan can be found at https://mrmc.amedd.army.mil/assets/docs/sse/SafetyAppendix093008.pdf. A Facility Safety

Plan from a research site/organization may have been received previously and approved by the USAMRMC. A list of organizations that have approved Facility Safety Plans can be found on the USAMRMC website at https://mrmc.amedd.army.mil/assets/docs/SSE/Facility_Safety_Plan_Approved_Institutions.pdf.

C. Research Involving Animal Use

Specific documents relating to the use of animals in the proposed research will be requested if the application is selected for funding (these documents should not be submitted with the application). The ACURO, a component of the USAMRMC ORP, must review and approve all animal use prior to the start of working with animals. PIs must submit the institutional animal use protocol, IACUC approval of that protocol, and a version of the animal use appendix titled "Research Involving Animals." For guidance on which version of the appendix to use, as well as links to both, visit the ACURO website at: https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.acuro_Animalappendix. Allow 2 to 3 months for regulatory review and approval processes for animal studies.

For additional information, send questions via email to ACURO (ACURO@amedd.army.mil).

D. Research Involving Human Subjects, Human Subjects Data, or Human Anatomical Substances

All USAMRMC-funded research involving human subjects and human anatomical substances must receive a USAMRMC Headquarters-level Administrative Review (note that this is distinct from an IRB review) and be approved by the USAMRMC ORP in addition to local IRBs.

Human subject research definitions, categories, and resource information may be found in the Human Subject Resource Document on the CDMRP eReceipt System website (https://cdmrp.org/Program_Announcements_and_Forms/). This information is a guide only; it is not intended to be a source for human subject protection regulations. Questions regarding applicable human subject protection regulations, policies, and guidance should be directed to the local IRB, the USAMRMC ORP (https://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.hrpo), and/or the U.S. Food and Drug Administration (FDA) as appropriate. For in-depth information refer to the ORP website (https://mrmc.detrick.army.mil/index.cfm?pageid=research_protections.overview) or the FDA website (http://www.fda.gov), or consult the local IRB.

ORP-specific language must be inserted into the consent form, and ORP reporting requirements must be included.

The ORP is mandated to ensure that all research complies with specific laws and directives governing research involving human subjects that is conducted or supported by the DoD. These laws and directives may require information in addition to that supplied to the local IRB.

During the regulatory review process for research involving human subjects, the ORP requirements must be addressed, and any changes to the already approved protocol must be approved as an amendment by the local IRB. It is strongly recommended that investigators carefully read the "Guidelines for Investigators" found at https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.hrpo. The time to approval depends greatly on adherence to these guidelines in a clear and comprehensive manner. If the protocol has not been submitted to the local IRB at the time of award negotiation, these guidelines should be considered before submission.

Documents related to the use of human subjects or human anatomical substances will be requested if the application is recommended for funding. ***Allow at least 2 to 3 months for regulatory review and approval processes for studies involving human subjects.***

Specific requirements for research involving human subjects or human anatomical substances can be found at https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.hrpo.

1. **Assurance of Compliance:** Each institution engaged in non-exempt human subjects research must have a current Department of Health and Human Services Office for Human Research Protection Federalwide Assurance or a DoD Assurance.

2. **Training:** Personnel involved in human subjects research must have appropriate instruction in the protection of human subjects. Documentation confirming completion of appropriate instruction may be required during the regulatory review process.

3. **Informed Consent Form:** The following must appear in the consent form:
   - A statement that the DoD or a DoD organization is funding the study.
   - A statement that representatives of the United States Army Medical Research and Materiel Command (or the DoD) are authorized to review research records.
   - In the event that a Health Insurance Portability and Accountability Act (HIPAA) authorization is required, representatives of the USAMRMC must be listed as one of the parties to whom private health information may be disclosed.

4. **Intent to Benefit:** Investigators must consider the requirements of Title 10 United States Code Section 980 (10 USC 980), which are applicable to DoD-sponsored research. 10 USC 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."

   Moreover, an individual not legally competent to consent (e.g., incapacitated individuals, cognitively impaired, minors) may not be enrolled as an experimental subject in a DoD-supported study 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. PIs should be aware that this law could make Phase I and placebo-controlled clinical trials problematic in these populations because of

the “intent to benefit” requirement whenever participation is sought of an experimental subject from whom consent must be obtained by the legally authorized representative.

Note that the definition of experimental subject is found in DODI 3216.02 and has a more narrow definition than human subject. Research with experimental subjects must involve an intervention or interaction where the primary purpose of the research is to collect data regarding the effects of the intervention or interaction.

10 USC 980 is only applicable to certain intervention studies. It does not apply to retrospective studies, observational studies, blood draws, and tissue collections. Contact the HRPO at 301-619-7550 for further clarification regarding applicability of 10 USC 980 to the proposed research project.

5. **Research Monitor Requirement:** An independent research monitor must be identified in the protocol for all greater than minimal risk research. A curriculum vitae or biographical sketch and human subjects protection training must be provided. The research monitor must have no apparent conflict of interest. The research monitor must not be under the supervision of the PI, other investigators, or research staff associated with the proposed research project. It is acceptable to provide appropriate compensation to the research monitor for his or her services.

   The role of the research monitor must be described in the protocol and be consistent with DoD guidance. For research with potential physical or psychological risk, monitors should be physicians, dentists, psychologists, nurses, or other healthcare providers capable of overseeing the progress of research protocols, especially issues of individual volunteer management and safety. Research monitors must be independent of the investigative team and possess sufficient educational and professional experience to serve as the volunteer advocate. Depending on the nature of the study, the monitor may be assigned to assess one or more of the following phases of research project: volunteer recruitment, volunteer enrollment, data collection, or data storage and analysis. The research monitor provides an independent evaluation of serious adverse events and unanticipated problems involving risk to subjects or others to the IRB and the ORP. The monitor may be assigned to discuss research progress with the PI, interview volunteers, consult on individual cases, or evaluate adverse event reports. Research monitors must promptly report discrepancies or problems to the IRB and the ORP. They shall have the authority to stop a research study in progress, remove individual volunteers from a study, and take whatever steps are necessary to protect the safety and well-being of research volunteers until the IRB can assess the research monitor’s report. Research with minimal physical or psychological risks may be determined to be greater than minimal risk for other reasons (e.g., sensitivity of identifiable data). In these cases, the research monitor should be selected based on the area of expertise required to appropriately monitor the research (e.g., someone with Information Technology expertise may be appropriate to monitor security of data stored in electronic systems).

6. **Military Personnel Volunteers:** The following is important information for research projects proposing to include military personnel as volunteers.

   - **Recruitment of Military Personnel:** Civilian investigators attempting to access military volunteer pools are advised to seek collaboration with a military investigator who will be familiar with service-specific requirements.

     A letter of support will be requested from the Commander of military facilities or units in which recruitment will occur or the study will be conducted. Some sites may also require that each volunteer seek written permission from their supervisor prior to participation in research studies. Special consideration must be given to the recruitment process for military personnel. The Chain of Command should not be involved in the recruitment of military personnel and should not encourage or order service members to participate in a research study. For greater than minimal risk research, an ombudsman must be employed when conducting group briefings with active duty personnel to ensure that volunteers understand that participation is voluntary; this ombudsman may be recommended in other situations as well, especially when young enlisted service members are recruited who are trained to follow orders. Service members are trained to act as a unit, so peer pressure should also be considered and minimized.

   - **Payment to Military Personnel:** Under 24 USC 30, payment to active duty military personnel for participation in research is limited to blood donation and may not exceed $50 per blood draw. Active duty research volunteers may not receive any other payment for participation in a research study unless they are off duty or on leave during the time they are participating in the protocol.

   - **Confidentiality for Military Personnel:** Confidentiality risk assessment for military personnel requires serious consideration of the potential to affect the military career. Medical and psychological diagnoses can lead to limitation of duties and/or discharge from active duty. Information regarding alcohol or drug abuse, drunk driving, and sexual or spousal abuse can lead to actions under the Uniform Code of Military Justice, including incarceration and dishonorable discharge.

7. **Site Visits:** The USAMRMC ORP HRPO conducts random site visits as part of its responsibility for compliance oversight.

   Accurate and complete study records must be maintained and made available to representatives of the USAMRMC as a part of their responsibility to protect human subjects in research. Research records must be stored in a confidential manner so as to protect the confidentiality of subject information.

   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.amedd.army.mil/index.cfm?pageid=research_protections.hrpo.

8. **Protocol Submission Format:** The ORP accepts protocol submissions in the format required by the local IRB. The IRB protocol application, if separate from the protocol

itself, should be included with protocol submissions. To avoid delays in the approval process, PIs should take the ORP guidelines into account when developing protocols for submission to the local IRB.

E. Clinical Trial Registry

PIs are required to register clinical trials individually on www.clinicaltrials.gov using a Secondary Protocol ID number designation of "CDMRP-CDMRP Log Number" (e.g., CDMRP-PC12####). If several protocols exist under the same application, the Secondary Protocol ID number must be designated "CDMRP-CDMRP Log Number-A, B, C, etc." (e.g., CDMRP-PC12####-A). Clinical trials must be registered prior to enrollment of the first patient. All trials that meet the definition on the National Institutes of Health database (see http://prsinfo.clinicaltrials.gov/, click on "Data Element Definitions") are required to register. Failure to do so may result in a civil monetary penalty and/or the withholding or recovery of grant funds as per U.S. Public Law 110-85.

APPENDIX 6

ACRONYM LIST

ACURO	Animal Care and Use Review Office
ADP	Automated Data Processing
AIBS	American Institute of Biological Sciences
AOR	Authorized Organizational Representative
AVI	Audio Video Interleave
CAGE	Commercial and Government Entity
CCR	Central Contractor Registry
CDMRP	Congressionally Directed Medical Research Programs
CFDA	Catalog of Federal Domestic Assistance
CFR	Code of Federal Regulations
COI	Conflict of Interest
CRADA	Cooperative Research and Development Agreement
CSI	Congressional Special Interest
DFARS	Department of Defense Federal Acquisition Regulation Supplement
DHHS	Department of Health and Human Services
DoD	Department of Defense
DODGAR	Department of Defense Grant and Agreement Regulations
DUNS	Data Universal Numbering System
EIN	Employer Identification Number
EPLS	Excluded Parties List System
ET	Eastern Time
F&A	Facilities and Administrative
FAR	Federal Acquisition Regulation
FDA	U.S. Food and Drug Administration
FY	Fiscal Year
G&A	General and Administrative
HIPAA	Health Information Portability and Accountability Act
HRPO	Human Research Protection Office
IACUC	Institutional Animal Care and Use Committee
IDE	Investigational Device Exemption
IND	Investigational New Drug
IP	Integration Panel
IRB	Institutional Review Board
JPEG	Joint Photographic Experts Group
M	Million
MB	Megabyte
MPEG	Moving Picture Experts Group
MTF	Medical Treatment Facility
OASD(HA)	Office of the Assistant Secretary of Defense for Health Affairs
OMB	Office of Management and Budget
ORP	Office of Research Protections
PDF	Portable Document Format

PI	Principal Investigator
POC	Point of Contact
SAIC	Science Applications International Corporation
SOW	Statement of Work
TIFF	Tagged Image File Format
TIN	Tax Identification Number
URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRMC	U.S. Army Medical Research and Materiel Command
USC	United States Code
WAV	Waveform Audio

APPENDIX 7

DOD/VA MTBI DEFINITION

THE ASSISTANT SECRETARY OF DEFENSE
1200 DEFENSE PENTAGON
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

OCT 1 2007

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)
ASSISTANT SECRETARY OF THE NAVY (M&RA)
ASSISTANT SECRETARY OF THE AIR FORCE (M&RA)

SUBJECT: Traumatic Brain Injury: Definition and Reporting

Reference: (a) Health Affairs Memorandum, "Consolidation of Traumatic Brain Injury Initiatives in the Department of Defense," dated March 23, 2007

Traumatic brain injury (TBI), whether mild, moderate, severe, or penetrating, is a significant health concern for the Department of Defense (DoD). To ensure a common understanding—as well as to design coordinated, coherent, high quality, and patient-centered programs—we must properly identify, document, and report those Service members who have suffered a TBI.

This memorandum establishes a common definition of TBI, severity of brain injury stratification, and method of data collection. These measures represent a major step toward unified TBI diagnosis and will lead to the advancement of therapeutic methods.

Services will identify TBI cases using the DoD definition of TBI (Attachment 1). Until automated mechanisms are established, Services will report all identified cases of TBI in accordance with Attachment 2. This requirement will become effective 60 days from the date of this memorandum. The Defense and Veterans Brain Injury Center (DVBIC) is designated as the single office of responsibility for the consolidation of all TBI-related incidence and prevalence information for DoD. The DVBIC will forward a monthly report (inclusive of Protected Health Information) to the office of the Deputy Assistant Secretary of Defense for Force Health Protection and Readiness.

The DoD's management of Service members with TBI is evolving rapidly. Definition and reporting are the foundation upon which this program must be based. Services can anticipate incremental policies and guidance addressing other components

of TBI management such as training, coding (International Classification of Diseases-9), evaluation and treatment. These efforts will culminate in a new DoD Center of Excellence for TBI and Psychological Health.

S. Ward Casscells, MD

Attachments:
As stated

cc:
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force
Medical Officer of the Marine Corps
Joint Staff Surgeon
Defense Health Board

DEFINITION OF TRAUMATIC BRAIN INJURY

A traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs, immediately following the event:

- Any period of loss of or a decreased level of consciousness;
- Any loss of memory for events immediately before or after the injury;
- Any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.);
- Neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient;
- Intracranial lesion.

External forces may include any of the following events: the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, a foreign body penetrating the brain, forces generated from events such as a blast or explosion, or other force yet to be defined.

The above criteria define the event of a traumatic brain injury (TBI). Sequelae of TBI may resolve quickly, within minutes to hours after the neurological event, or they may persist longer. Some sequelae of TBI may be permanent. Most signs and symptoms will manifest immediately following the event. However, other signs and symptoms may be delayed from days to months (e.g., subdural hematoma, seizures, hydrocephalus, spasticity, etc.). Signs and symptoms may occur alone or in varying combinations and may result in a functional impairment. These signs and symptoms are not better explained by pre-existing conditions or other medical, neurological, or psychological causes except in cases of an exacerbation of a pre-existing condition. These generally fall into one or more of the three following categories:

- <u>Physical</u>: Headache, nausea, vomiting, dizziness, blurred vision, sleep disturbance, weakness, paresis/plegia, sensory loss, spasticity, aphasia, dysphagia, dysarthria, apraxia, balance disorders, disorders of coordination, seizure disorder.

- Cognitive: Attention, concentration, memory, speed of processing, new learning, planning, reasoning, judgment, executive control, self-awareness, language, abstract thinking.

- Behavioral/emotional: Depression, anxiety, agitation, irritability, impulsivity, aggression.

Note: The signs and symptoms listed above are typical of each category but are not an exhaustive list of all possible signs and symptoms.

SEVERITY OF BRAIN INJURY STRATIFICATION:

Not all individuals exposed to an external force will sustain a TBI. TBI varies in severity, traditionally described as mild, moderate and severe. These categories are based on measures of length of unconsciousness, post-traumatic amnesia.

The trauma may cause structural damage or may produce more subtle damage that manifests by altered brain function, without structural damage that can be detected by traditional imaging studies such as Magnetic Resonance Imaging or Computed Tomography scanning. In addition to traditional imaging studies, other imaging techniques such as functional magnetic resonance imaging, diffusion tensor imaging, positron emission tomography scanning, as well as electrophysiological testing such as electroencephalography may be used to detect damage to or physiological alteration of brain function. In addition, altered brain function may be manifest by altered performance on neuropsychological or other standardized testing of function.

Acute injury severity is determined at the time of the injury, but this severity level, while having some prognostic value, does not necessarily reflect the patient's ultimate level of functioning. It is recognized that serial assessments of the patient's cognitive, emotional, behavioral and social functioning is required.

- The patient is classified as mild/moderate/severe if he or she meets any of the criteria below within a particular severity level. If a patient meets criteria in more than one category of severity, the higher severity level is assigned.

- If it is not clinically possible to determine the brain injury level of severity because of medical complications (e.g., medically induced coma), other severity markers are required to make a determination of the severity of the brain injury.

Mild	Moderate	Severe
Normal structural imaging	Normal or abnormal structural imaging	Normal or abnormal structural imaging
LOC = 0–30 min*	LOC >30 min and < 24 hours	LOC > 24 hrs
AOC = a moment up to 24 hrs	AOC >24 hours. Severity based on other criteria	
PTA = 0–1 day	PTA >1 and <7 days	PTA > 7 days

AOC – Alteration of consciousness/mental state
LOC – Loss of consciousness
PTA – Post-traumatic amnesia

* An inconsistency currently exists between this published guidance and the published V codes for mild TBI when loss of consciousness is between 30 and 59 minutes. Until this inconsistency is resolved, Services are to report in the attached format using the criteria published above.

It is recognized that the cognitive symptoms associated with post-traumatic stress disorder (PTSD) may overlap with symptoms of mild TBI. Differential diagnosis of brain injury and PTSD is required for accurate diagnosis and treatment.