Program Announcement

for the

Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Joint Program Committee 8/Clinical and Rehabilitative Medicine Research Program

Vision Research Program

Clinical Trial Award

Funding Opportunity Number: W81XWH-15-VRP-CTA

Catalog of Federal Domestic Assistance Number: 12.420

Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Deadline:** 5:00 p.m. Eastern time (ET), December 2, 2015
- **Application Submission Deadline:** 11:59 p.m. ET, December 16, 2015
- **End of Application Verification Period:** 5:00 p.m. ET, December 18, 2015
- **Peer Review:** February 2016
- **Programmatic Review:** April 2016

The CDMRP eReceipt System has been replaced with the electronic Biomedical Research Application Portal (eBRAP). Principal Investigators and organizational representatives should register in eBRAP as soon as possible. All pre-applications must be submitted through eBRAP. In addition, applications submitted through Grants.gov will now be available for viewing, modification, and verification in eBRAP prior to the end of the application verification period.

This Program Announcement/Funding Opportunity is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2015/2016 (FY15/16) Vision Research Program (VRP) are being solicited for the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate, by the U.S. Army Medical Research Acquisition Activity (USAMRAA). As directed by the Office of the Assistant Secretary of Defense for Health Affairs [OASD(HA)], the DHA RDA Directorate manages and executes the Defense Health Program (DHP) Research, Development, Test, and Evaluation (RDT&E) appropriation. This Program Announcement/Funding Opportunity and subsequent awards will be managed and executed by the Congressionally Directed Medical Research Programs (CDMRP) with strategic oversight from Joint Program Committee 8/Clinical and Rehabilitative Medicine Research Program (JPC-8/CRMRP). The VRP was initiated in FY09 to fund innovative research that has the potential to make a significant impact on improving the health and well-being of military Service members, Veterans, and other individuals living with visual dysfunction. Appropriations for the VRP from FY09 through FY14 totaled $45.2 million (M). The FY15 appropriation is $10M.

The FY15/16 VRP challenges the scientific community to design innovative research that will foster new directions for, and address neglected issues in, the field of vision research. Applications from investigators within the military Services, and applications involving multidisciplinary collaborations among academia, industry, the military Services, the U.S. Department of Veterans Affairs (VA), and other Federal Government agencies are highly encouraged.

One of six major program areas within the DHA RDA, the JPC-8/CRMRP seeks to ethically and responsibly develop long-term strategies to find, evaluate, and fund cutting edge research in reconstruction, rehabilitation, and definitive care for injured Warfighters to improve the standard of care and outcomes, return Service members to full form and function, and ultimately restore the Warfighter to duty and improve his or her quality of life. The program has multiple initiatives to achieve its goals, including improving prosthetic function, enhancing self-regenerative capacity, improving limb/organ transplant success, creating full functioning limbs/organs, repairing damaged eyes, treating visual dysfunction following injury, improving pain management, and enhancing rehabilitative care. Additional information about JPC-8/ CRMRP can be found at: https://crmrp.amedd.army.mil/.

B. FY15/16 VRP Capability Gaps and Focus Areas

FY15/16 VRP CTA Capability Gaps

To meet the intent of the FY15/16 VRP Clinical Trial Award (CTA), the research proposals ***must*** address one or more of the Capability Gaps listed below:

- Inadequate mitigation and treatment of damage to ocular structures and the visual system consequent to military-relevant injuries and diseases incident to military service. Research into ocular damage that occurs in the general public will also be considered, as there may be similarities and related treatments in the two populations.

- Inadequate treatments and technologies for injuries and diseases to ocular structures and visual systems, to include optic neuropathy, retinal injury, lid and adnexal injuries, and ocular polytrauma
- Inadequate strategies and techniques for controlling scarring and/or pathological healing response in traumatized ocular tissues

- Inadequate vision restoration and regeneration
  - Inability to restore form and function of lids, adnexal, orbital, and ocular tissues (optic nerve, cornea, retina, and uvea) following injury
  - Inadequate vision surrogates and appropriate rehabilitation
- Lack of knowledge, capabilities, and equipment for early responders to diagnose and mitigate military-relevant eye injuries and diseases in austere or remote environments
  - Lack of methods and or devices to assist in the location of entrance wounds and rupture sites in traumatic eye injuries
  - Lack of portable diagnostic tools and technologies for field use to detect ocular injuries and diseases

FY15/16 VRP CTA Focus Areas

The five Focus Areas are listed below and have been developed to address the Capability Gaps listed above. All applications are ***highly encouraged*** to address at least one of the following Focus Areas:

- Phase I/Phase II clinical trials to evaluate safety and/or efficacy of treatments or technologies to reduce/control scarring and/or pathological healing response(s) after military-relevant ocular/visual system injury
- Phase I/Phase II clinical trials to evaluate safety and/or efficacy of treatments or technologies restoring form and function to: (1) orbit and ocular tissues (optic nerve, retina, and uvea), (2) eyelid, and/or (3) adnexal structures
- Phase I/Phase II clinical trials to demonstrate feasibility and safety and/or efficacy of vision surrogates for those with low or no vision post-injury and appropriate rehabilitation
- Phase I/Phase II clinical trials for evaluation of technologies to identify the location of entrance wounds and rupture sites in traumatic eye injuries
- Phase I/Phase II clinical trials for evaluation of technologies to detect and quantify white blood cells, red blood cells and proteins in both the aqueous and vitreous humor

C. Award Information

The FY15/16 VRP CTA supports research with the potential to have a major impact on the treatment or management of visual injury and/or dysfunction. ***Funding from this award mechanism must support a clinical trial and should not be used for preclinical research studies. PIs seeking funding for preclinical research should apply to the FY15/16 VRP Technology/Therapeutic Development Award mechanism (W81XWH-15-VRP-TTDA).***

Applications proposing research outside of the Capability Gaps listed above should ***not*** be submitted in response to this Program Announcement/Funding Opportunity.

A clinical trial is defined as a prospective accrual of human subjects where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention, or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the human subject of that intervention or interaction. The term "human subjects" is used in this Program Announcement/Funding Opportunity to refer to individuals who will be recruited for or who will participate in the proposed clinical trial. For more information, a Human Subject Resource Document is provided at https://ebrap.org/eBRAP/public/Program

In keeping with the intent of this award mechanism, at the end of the period of performance this work should show clear progress toward the next stage of implementation (i.e., Phase II clinical trials, U.S. Food and Drug Administration (FDA) clearance for a medical device, etc.).

If the clinical trial involves the use of a drug that has not been approved by the FDA for the proposed investigational use, evidence that an Investigational New Drug (IND) exemption application that meets all requirements under the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312) has been submitted or will be submitted to the FDA ***within 60 days of award*** is required. If the investigational product is a device, evidence that an Investigational Device Exemption (IDE) application that meets all requirements under 21 CFR 812 has been submitted or will be submitted to the FDA ***within 60 days of award***, or that the device is exempt from an IDE, is required. The Government reserves the right to withdraw funding if the IND or IDE application has not been submitted to the FDA within 60 days of the Department of Defense (DoD) award date or if the documented status of the IND or IDE has not been obtained within 6 months of the award date.

The following are important aspects of submission for the FY15/16 VRP CTA:

- The proposed clinical trial is expected to begin no later than 12 months after the award date.
- The proposed intervention to be tested should offer significant potential impact for military Service members, Veterans, and other individuals living with visual dysfunction.
- Inclusion of preliminary data relevant to the proposed research project is required.
- The proposed research project must be based on sound scientific rationale that is established through logical reasoning and critical review and analysis of the literature.
- The application should describe the planned indication for the product label, if appropriate, and include an outline of the development plan required to support that indication.
- The application should demonstrate availability of, and access to, a suitable patient population that will support a meaningful outcome for the study. The PI should discuss how accrual goals will be achieved and how standards of care may impact the study population.

- The application should demonstrate documented availability of, and access to, the drug/ compound, device, and/or other materials needed, as appropriate. The quality of the product should be commensurate with FDA manufacturing standards applicable to the type and phase of product being developed (i.e., Quality System Regulation, Good Manufacturing Practices).
- The proposed clinical trial design should include clearly defined and appropriate endpoints and follow Good Clinical Practice (GCP) guidelines.
- The application should include a clearly articulated statistical analysis plan, appropriate statistical expertise on the research team, and a power analysis reflecting sample size projections that will clearly answer the objectives of the study.
- The application should include a clearly articulated data management plan and use of an appropriate database to safeguard and maintain the integrity of the data.
- The application should include a clearly articulated safety management plan, outlining how safety pharmacovigilance will be conducted, as applicable.
- The application should include a clearly articulated clinical monitoring plan, outlining how the study will be monitored for GCP compliance.
- The application should include a study coordinator(s) who will guide the clinical protocol through the local Institutional Review Board (IRB) of record and other Federal agency regulatory approval processes, coordinate activities from all sites participating in the trial, and coordinate participant accrual.
- The application should include a Transition Plan (including potential funding and resources) showing how the product will progress to the next clinical trial phase and/or delivery to the market after the successful completion of the VRP CTA.
- The application should clearly demonstrate strong institutional support.
- The application should acknowledge the commitment to filing the study in the National Institutes of Health (NIH) clinical trials registry, www.clinicaltrials.gov.

Research Involving Human Anatomical Substances, Human Subjects, or Human Cadavers: All DoD-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local IRB of record. Local IRB approval at the time of submission is ***not*** required. The HRPO is mandated to comply with specific laws and requirements governing all research involving human anatomical substances, human subjects, or human cadavers that is supported by the DoD. These laws and requirements will necessitate information in addition to that supplied to the IRB. ***Allow a minimum of 2 to 3 months for HRPO regulatory review and approval processes***. The HRPO reviews and approves the participation of each site in the clinical trial. Refer to the General Application Instructions, Appendix 5, and the Human Subject Resource Document available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for additional information.

If the IRB determines that human subjects may be exposed to greater-than-minimal-risk in a trial, the DoD requires an independent research monitor with expertise consistent with the nature of risk(s) identified within the research protocol. If applicable, please refer to the General Application Instructions, Appendix 5, for more information on study reporting authorities and responsibilities of the research monitor.

Multi-Institutional Research: Multi-institutional projects are encouraged when combining the resources of two or more organizations will strengthen the research application. If the proposed research is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, must be included. A separate intellectual and material property plan agreed upon by all participating institutions is also required for multi-institutional research. Participating institutions must be willing to resolve potential intellectual and material property issues and to remove any barriers that may interfere with achieving high levels of cooperation to ensure successful completion of this award.

DoD Collaboration and Alignment Encouraged: Relevance to the health care needs of the Armed Forces, their family members, and/or the U.S. Veteran population is a key feature of this award. Therefore, PIs are strongly encouraged to collaborate, integrate, and/or align their research projects with military and/or VA research laboratories and programs. The following websites may be useful in identifying information about ongoing DoD areas of research interest:

Air Force Research Laboratory
http://www.wpafb.af.mil/afrl

Clinical and Rehabilitative Medicine Research Program
https://crmrp.amedd.army.mil/

Congressionally Directed Medical Research Programs
http://cdmrp.army.mil

Defense Advanced Research Projects Agency
http://www.darpa.mil/

Defense Technical Information Center
http://www.dtic.mil

Naval Health Research Center
http://www.med.navy.mil/sites/nhrc

Naval Medical Research Center
http://www.med.navy.mil/sites/nmrc

Navy and Marine Corps Public Health Center
http://www.nmcphc.med.navy.mil/

Office of Naval Research
http://www.med.navy.mil/

Office of the Under Secretary of Defense for Acquisition, Technology and Logistics
http://www.acq.osd.mil/

U.S. Army Institute of Surgical Research
http://www.usaisr.amedd.army.mil/

U.S. Army Medical Research Acquisition Activity
http://www.usamraa.army.mil

U.S. Army Medical Research and Materiel Command
https://mrmc.amedd.army.mil

U.S. Army Research Laboratory
http://www.arl.army.mil

U.S. Naval Research Laboratory
https://www.nrl.navy.mil

U.S. Department of Veterans Affairs, Office of Research and Development
www.research.va.gov

Use of Military and VA Populations or Resources: If the proposed research involves access to military and/or VA population(s) and/or resource(s), the PI is responsible for establishing access. If possible, access to target military and/or VA patient population(s) should be confirmed at the time of application submission. A letter of support, signed by the lowest ranking person with approval authority, should be included as part of Attachment 2 for studies involving Service members, Veterans, military and/or VA-controlled study materials, and military and/or VA databases. See Section II.C., Full Application Submission Content, Supporting Documentation.

The JPC-8/CRMRP and CDMRP intend that information, data, and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 3, Section L.

D. Eligibility Information

- PIs must be at or above the level of Assistant Professor (or equivalent).
- Cost sharing/matching is not an eligibility requirement.
- Eligible investigators must apply through an organization. Organizations eligible to apply include national, international, for-profit, nonprofit, public, and private organizations.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

- The maximum period of performance is **4** years.
- The anticipated total (direct and indirect) costs budgeted for the entire period of performance will not exceed **$3M**. Indirect costs are to be budgeted in accordance with the organization's negotiated rate. No budget will be approved by the Government exceeding **$3M** total costs or using an indirect rate exceeding the organization's negotiated rate.
- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum **4** years.

Refer to the General Application Instructions, Section II.C.5., for budget regulations and instructions for the Research & Related Budget. ***For all Federal agencies or organizations collaborating with Federal agencies, budget restrictions apply as are noted in Section II.C.5. of the General Application Instructions***.

For this award mechanism, direct costs must be requested for:

- Travel costs for the PI(s) to disseminate project results at a one-day DoD VRP review meeting. For planning purposes, it should be assumed that the meeting will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary
- Equipment
- Research-related subject costs
- Clinical research costs
- Support for multidisciplinary collaborations
- Travel between collaborating organizations
- Travel costs to attend scientific/technical meetings in addition to the required meeting described above

Intramural (DoD), other Federal agency, and extramural investigators are encouraged to apply to this Program Announcement/Funding Opportunity. An intramural investigator is defined as a DoD military or civilian employee working within a DoD laboratory or medical treatment facility, or working in a DoD activity embedded within a civilian medical center. Intramural applicants and collaborators are reminded to coordinate receipt and commitment of funds through their respective resource managers. It is permissible for an intramural investigator to be named as a collaborator on an application submitted by an extramural investigator. ***In such cases, the extramural investigator must include a letter from the intramural collaborator's Commander or Commanding Officer that authorizes the involvement of the intramural collaborator.***

As required of all applicants to this Program Announcement/Funding Opportunity, if PIs from Federal agencies submit applications, they must submit through Grants.gov. Therefore, Federal applicants must be familiar with Grants.gov requirements, including the need for an active System for Award Management (SAM) registration and a Data Universal Numbering System (DUNS) number. Refer to Section II.A. of the General Application Instructions for further information regarding Grants.gov requirements.

Awards to extramural organizations will consist solely of assistance agreements (Cooperative Agreements and Grants). Awards to intramural agencies and other Federal agencies may be executed through a direct fund transfer (e.g., the Military Interdepartmental Purchase Request [MIPR] or Funding Authorization Document [FAD] process). Direct transfer of funds from the recipient to a Federal agency is not allowed except under very limited circumstances. Refer to the General Application Instructions, Section II.C.5. Research & Related Budget, for additional information on budget considerations for applications involving Federal agencies.

The CDMRP expects to allot approximately $6M of the $10M FY15 VRP appropriation to fund approximately 2 Clinical Trial Award applications, depending on the quality and number of applications received. In addition to the FY15 appropriation, it is anticipated that up to $6M in FY16 funds may be available to fund approximately 2 additional awards. As of the release date of this Program Announcement/Funding Opportunity, the FY16 Defense Appropriations Bill has not been passed and there is no guarantee that any additional funds will be made available to support this program. The funding estimated for this Program Announcement/Funding Opportunity is approximate and subject to realignment. Funding of

applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of Federal funds for this program.

II. SUBMISSION INFORMATION

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities in different programs or funding agencies is allowed, however, it must be noted in the application under PI Previous/Current/Pending Support (see Section II.C.3, Research & Related Senior/Key Person Profile). Failure to provide notification will result in administrative withdrawal of the duplicative application. NOTE: Funding can only be accepted from one funding source for the same application.

Submission is a two-step process requiring both (1) pre-application submission through the electronic Biomedical Research Application Portal (eBRAP) (https://eBRAP.org/) and (2) application submission through Grants.gov (http://www.grants.gov/). Refer to the General Application Instructions, Section II.A. for registration and submission requirements for eBRAP and Grants.gov.

eBRAP is a multifunctional web-based system that allows PIs to submit their pre-applications electronically through a secure connection, to view and edit the content of their pre-applications and full applications, to receive communications from the CDMRP, and to submit documentation during award negotiations and period of performance. A key feature of eBRAP is the ability of an organization's representatives and PIs to view and modify the Grants.gov application submissions associated with them. eBRAP will validate Grants.gov application files against the specific Program Announcement/Funding Opportunity requirements, and discrepancies will be noted in an email to the PI and in the Full Application Files tab in eBRAP. It is the applicant's responsibility to review all application components for accuracy as well as ensure proper ordering as specified in this Program Announcement/Funding Opportunity.

PIs should ensure that their name and email address are the same as the name and email address that will be provided on the SF-424 Form of the Grants.gov application package submitted to Grants.gov. The organization, Business Officials, PI(s), and eBRAP log number named in the full application submitted to Grants.gov must match those named in the pre-application in eBRAP. Application viewing, modification, and verification in eBRAP is strongly recommended, but not required. The Project Narrative and Budget cannot be changed after the application submission deadline. Any other application component cannot be changed after the end of the application verification period.

A. Where to Obtain the Grants.gov Application Package

To obtain the Grants.gov application package, including all required forms, perform a basic search using the Funding Opportunity Number W81XWH-15-VRP-CTA in Grants.gov (http://www.grants.gov/).

B. Pre-Application Submission Content

All pre-application components must be submitted by the PI through eBRAP (https://eBRAP.org/).

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.

The pre-application consists of the following components, which are organized in eBRAP by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
  - Enter contact information for the PI. Enter the organization's Business Official responsible for sponsored program administration (the "person to be contacted on matters involving this application" in Block 5 of the Grants.gov SF-424 Form). The Business Official must either be selected from the eBRAP list or invited in order for the pre-application to be submitted.
  - It is recommended that PIs identify an Alternate Submitter in the event that assistance with pre-application submission is needed.
- **Collaborators and Key Personnel – Tab 3**
  - Enter the name, organization, and role of all collaborators and key personnel associated with the application.
  - FY15/16 VRP Integration Panel (IP) members should not be involved in any pre-application or application. For questions related to IP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@eBRAP.org or 301-682-5507.
- **Conflicts of Interest (COIs) – Tab 4**
  - List all individuals other than collaborators and key personnel who may have a COI in the review of the application (including those with whom the PI has a personal or professional relationship).
- **Pre-Application Files – Tab 5**
  - **Letter of Intent (LOI) (one-page limit):** Provide a brief description of the research to be conducted. Include the FY15/16 VRP CTA Capability Gap(s) and, if applicable, Focus Area(s) under which the application will be submitted. LOIs are used for program planning purposes only (e.g., reviewer recruitment) and will not be reviewed during either the peer or programmatic review sessions.

- **Submit Pre-Application – Tab 6**
  - This tab must be completed for the pre-application to be accepted and processed.

C. Full Application Submission Content

Full applications will not be accepted unless the PI has submitted a pre-application.

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

Each application submission must include the completed Grants.gov application package provided in Grants.gov for this Program Announcement/Funding Opportunity. The Grants.gov application package is submitted by the Authorized Organizational Representative through the Grants.gov portal (http://www.grants.gov/).

Note: The Project Narrative and Budget Form cannot be changed after the application submission deadline. If either the Project Narrative or the budget fails eBRAP validation or if the Project Narrative or Budget Form needs to be modified, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID ***prior to the application submission deadline***.

Grants.gov application package components: For the Clinical Trial Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF-424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

2. **Attachments Form**

   Each attachment to the Grants.gov application forms must be uploaded as an individual PDF file in accordance with the formatting guidelines listed in Appendix 2 of the General Application Instructions. For all attachments, ensure that the file names are consistent with the guidance. Grants.gov will reject attachments with file names longer than 50 characters or incorrect file names that contain characters other than the following: A-Z, a-z, 0-9, underscore, hyphen, space, and period. In addition, Grants.gov has file size limits that may apply in some circumstances. Individual attachments may not exceed 20 MB and the file size for the entire Grants.gov application package may not exceed 200 MB.

   The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6-8 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

   - **Attachment 1: Project Narrative (15-page limit): Upload as "ProjectNarrative.pdf."** The page limit of the Project Narrative applies to text

and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

Describe the proposed project in detail using the outline below.

- **Background:** State the relevance of the research to at least one of the FY15/16 Capability Gaps and, if applicable, FY15/16 VRP CTA Focus Area(s) and explain the applicability of the proposed findings. Present the ideas and reasoning behind the proposed work. ***Include preliminary and/or published data that are relevant to vision dysfunction and the proposed research project.***

  Describe in detail the rationale for the study. Provide a literature review and describe the preliminary studies and/or preclinical data that led to the development of the proposed clinical trial. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for other indications (as applicable). The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

  If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source of prior funding. Specifically identify the portions of the study that will be supported with funds from this award.

- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/ hypotheses.

- **Study Design:** Describe the type of study to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate.

  - Identify the intervention to be tested and describe the projected outcomes.
  - Define the study variables, outline why they were chosen, and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
  - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
  - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the

specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).

- If using psychometric measures, describe their reliability and validity.

- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects to be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study.

- **Attachment 2: Supporting Documentation. Start each document on a new page. Combine and upload as a single file named "Support.pdf."** If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested will result in the removal of those items or may result in administrative withdrawal of the application.***

  - References Cited: List the references cited (including URLs if available) in the Project Narrative 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).

  - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.

  - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate whether or not Government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present Government award under which the facilities or equipment items are now accountable. There is no form for this information.

  - Publications and/or Patent Abstracts: Include a list of relevant publication URLs and/or patent abstracts. If publications are not publicly available, then copies of up to five published manuscripts may be included in Attachment 2. Extra items will not be reviewed.

  - Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, confirming the laboratory space, equipment, and other resources available for the project. 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.

- Letters of Collaboration: Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
- Letter(s) of Support for Use of Military and VA Populations or Resources (if applicable): Provide a letter(s) signed by the lowest ranking person with approval authority for studies involving military Service members, Veterans, military and/or VA-controlled study materials, and military and/or VA databases.
- Intellectual Property
  - Background and Proprietary Information: All software and data first produced under the award are subject to a Federal purpose license. Provide a list of all background intellectual property to be used in the project or provide a statement that none will be used. If applicable, state and identify the proprietary information that will be provided to the Government and indicate whether the applicant will require a waiver of the Federal purpose license.
  - Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.
- Data and Research Resources Sharing Plan: Describe how data and resources generated during the performance of the project will be shared with the research community. Refer to the General Application Instructions, Appendix 3, Section L for more information about the CDMRP expectations for making data and research resources publicly available.
- Quad Chart: The Quad Chart template is a one-page PowerPoint file that must be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm, completed and saved as a PDF file using Adobe Acrobat Reader.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf."** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Proprietary or confidential information should not be included. Technical abstracts should be written using the outline below.

  - **Background:** State how the proposed research addresses an FY15/16 VRP CTA Capability Gap and, if applicable, Focus Area. Present the ideas and rationale behind the proposed work.
  - **Objective/Hypothesis:** State the objective/hypothesis to be tested. Provide evidence 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 and Military Benefit:** Briefly explain how the proposed project will have an immediate or potential long-term impact on the health and well-being of military Service members, Veterans, and other individuals living with visual dysfunction.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf."** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  The lay abstract is an important component of the application review process because it addresses issues of particular interest to the advocate community.

  Lay abstracts should be written using the outline below. Proprietary or confidential information should ***not*** be included. *Do not duplicate the technical abstract.*]

  - Describe the objectives and rationale for the application in a manner that will be readily understood by readers without a background in science or medicine.
  - Describe the ultimate applicability and impact of the research.
    - What types of patients will it help, and how will it help them? Include the current available statistics to the related injury/condition.
    - What are the potential clinical applications, benefits, and risks?
    - What is the projected timeline it may take to achieve the expected patient-related outcome?
    - What are the likely contributions of the proposed research project to advancing the field of vision dysfunction?
    - Briefly describe how the proposed project will benefit military Service members, Veterans, and other individuals living with visual dysfunction.

- **Attachment 5: Statement of Work (SOW) (three-page limit): Upload as "SOW.pdf."** The suggested SOW format and examples specific to different types of research projects are available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). For the **Clinical Trial Award** mechanism, use the SOW format example titled "SOW (Statement of Work) for Clinical Research." The SOW must be in PDF format prior to attaching. Refer to the General Application Instructions, Section II.C.3., for detailed guidance on creating the SOW.

- **Attachment 6: Human Subject Recruitment and Safety Procedures (no page limit): Upload as "HumSubProc.pdf."** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  a. Study Population: Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Demonstrate that the research team has access to the proposed study population. Furthermore, discuss past efforts in recruiting human subjects from the target population for

previous clinical trials (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays. Include justification of any age, race, ethnicity, or sex limitations provided. ***For clinical trials proposing to include military personnel, please refer to the General Application Instructions, Appendix 5, for more information.***

b. Inclusion/Exclusion Criteria: List the inclusion and exclusion criteria for the proposed clinical trial. Inclusion/exclusion criteria should take into consideration the specific risk profile of the studies to be conducted and the standard of care for that patient population. Provide detailed justification for exclusions.

Inclusion of Women and Minorities in Study. Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and Congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Include an appropriate justification if women and/or minorities will be excluded from the clinical trial.

c. Description of the Recruitment Process: Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification).

- Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them.
- Include a detailed description of and justification for the compensation plan if the human subjects will be compensated for participation in the study.
- Describe the recruitment and advertisement materials. The recruitment materials should not be coercive or offer undue inducements and should accurately reflect the study.

d. Description of the Informed Consent Process: Specifically describe the plan for obtaining informed consent from human subjects.

- ***For the proposed study, provide a draft, in English, of the Informed Consent Form.***
- Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial.
- Include information regarding the timing and location of the consent process.
- Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.

- Address how privacy and time for decision making will be provided and whether or not the potential human subject will be allowed to discuss the study with anyone before making a decision.
- Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.
- Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. Note: The PI must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial to be in compliance with Title 10 United States Code Section 980 (10 USC 980) (http://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf). If applicable, please refer to the General Application Instructions, Appendix 5, for more information.
- ***Assent.*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

e. Screening Procedures: List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry. Please note that some screening procedures may require a separate consent or a two-stage consent process. Informed consent must be obtained prior to initiation of any procedures for the purpose of determining eligibility.

f. Risks/Benefits Assessment:

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. Study risks include any risks that the human subject is subjected to as a result of participation in the clinical trial. Consider psychological, legal, social, and economic risks as well as physical risks. If the risks are unknown, this should be stated. If applicable, any potential risk to the study personnel should be identified.
- **Risk management and emergency response:**
  - Describe how safety surveillance and reporting to the IRB and FDA (if applicable) will be managed and conducted.
  - Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values.

- Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, to include who will be responsible for the cost of such care.
- Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention).
- Describe any special care (e.g., wound dressing assistance, transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study.
- For a trial in which the IRB determines there is greater than minimal risk to human subjects, the DoD requires an independent research monitor with expertise consonant with the nature of risk(s) identified within the research protocol. If applicable, please refer to the General Application Instructions, Appendix 5, for more information on study reporting authorities and responsibilities of the research monitor.

- **Potential benefits:** Describe known and potential benefits of the study to the human subject, a specific community, or society.

- **Attachment 7: Intervention (no page limit): Upload as "Intervention.pdf."** The Intervention attachment should include the components listed below.

  a. Description of the Intervention: As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described.

  Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety of the intervention.

  b. Study Procedures: Describe the interaction with the human subject to include the study intervention that he/she will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Discuss how compliance with Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and other regulatory considerations will be established, monitored, and maintained, as applicable.

  c. Clinical Monitoring Plan: Describe how the study will be conducted by and monitored for ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) Good Clinical Practices (GCP) compliance, by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types

of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 8: Data Management (no page limit): Upload as "Data_Manage.pdf."** The Data Management attachment should include the components listed below.

  a. Data Management: Describe all methods used for data collection to include the following:

  - **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.
  - **Confidentiality:**
    - Explain measures taken to protect the privacy of human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.
    - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of the DoD are eligible to review study records.
    - Address requirements for reporting sensitive information to state or local authorities.
  - **Data capture, verification, and disposition:** Describe how data will be captured and verified. Describe where data (both electronic and hard copy) will be stored, who will keep the data, how the data will be stored, the process for locking the database at study completion, and the length of time data will be stored. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. For FDA-regulated studies, compliance with 21 CFR 11 is required.
  - **Sharing study results:** In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether or not the results of screening and/or study participation will be shared with human subjects or their primary care provider, to include results from any screening or diagnostic tests performed as part of the study.

  b. Laboratory Evaluations:

  - **Specimens to be collected, schedule, and amount:** All specimens that will be collected for study purposes must be clearly stated. The collection schedule and amount of material collected must also be clearly described.
  - **Evaluations to be made:** Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects).

- **Storage:** Describe specimen storage, to include location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline the plan to store specimens for future use to include considerations for informed consent and providing human subjects with an opportunity to decline participation in the study.
- **Labs performing evaluations and special precautions:** Identify the laboratory performing each evaluation, as well as any special precautions that should be taken in handling the samples. Special precautions that should be taken by the human subject before, during, or after the laboratory procedure should be clearly defined. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Attachment 9: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as "Personnel.pdf."** The Study Personnel and Organization attachment should include the components listed below.

  a. **Organizational Chart:** Provide an organizational chart identifying key members of the study team including institution/center/department and name each person's position on the project. If applicable, include any external consultants or other experts who will assist with FDA applications. While there is no specified format for this information, a table(s) or diagram is recommended.

  b. **Study Personnel Description:** Briefly describe the roles of the individuals listed in the organizational chart on the project. Describe relevant experience and qualifications that demonstrate appropriate expertise for the given role. A research monitor (external to the study) and study coordinator(s) should be included.

  c. **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial is multi-institutional, plans for communication and data transfer between the collaborating institutions, as well as how data, specimens, and/or imaging products obtained during the study will be handled, should be included. Provide a plan for real-time communication among collaborating institutions (if applicable).

- **Attachment 10: Surveys, Questionnaires, and Other Data Collection Instruments, if applicable (no page limit): Upload as "Surveys.pdf."** The Surveys, Questionnaires, and Other Data Collection Instruments attachment should include a copy of the most recent version of surveys, questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study.

- **Attachment 11: Impact and Military Benefit Statement (two-page limit): Upload as "ImpactMilBen.pdf."** Describe the short- and long-term impact of this study on the field of vision research, patient care, and/or quality of life, including an

assessment of the likelihood that a successful outcome of the proposed research project will lead to a practical application in individuals recovering from military-relevant injuries and diseases incident to military service as well as injuries and diseases occurring in the general public. Address the impact on one or more FY15/16 VRP Capability Gaps and, if applicable, CTA Focus Areas. Although not all-inclusive, the following are examples of ways in which research projects may have an impact, if successful:

- Describe how the research has the potential to advance the field of vision research.
- Describe how the intervention has the potential to change the standard of care.
- Describe how the research contributes to the development or validation of evidence-based policy or guidelines for patient evaluation and care.
- Describe any relevant controversies or treatment issues that will be addressed by the proposed clinical trial.
- Describe any potential issues that might limit the impact of the proposed clinical trial.
- Describe how the intervention represents an improvement over currently available interventions and/or standards of care.
- If the active duty military, Veteran, or military family member population(s) will be used in the proposed research project, describe the population(s), the appropriateness of the population(s) for the proposed research, and the feasibility of using the population. If a non-military population will be used for the proposed research project, explain how the population simulates the targeted population.

- **Attachment 12: Transition Plan (one-page limit). Upload as "Transition.pdf."** Provide information on the methods and strategies proposed to move the product or knowledge outcomes to the next phase of clinical trials, commercialization, and/or delivery to the civilian or military market after successful completion of the award. The transition plan should include the components listed below.
  - The planned indication for the product label, if appropriate, and an outline of the development plan required to support that indication.
  - Details of the funding strategy that will be used to bring the outcomes to the next level of development and/or commercialization (e.g., specific potential industry partners, specific funding opportunities to be applied for).
  - For knowledge products, a description of how the knowledge will be further developed, disseminated, and incorporated into clinical care.
  - A description of collaborations and other resources that will be used to provide continuity of development.
  - A brief schedule and milestones for bringing the outcome(s) to the next phase of clinical trials, commercialization, and/or delivery to the military or civilian

market, including when it can be anticipated to be transitioned to an industry partner or approved by the FDA, if applicable.

- The involvement of appropriate intellectual property, licensing, and/or business professionals.
- A risk analysis for cost, schedule, manufacturability, and sustainability.

- **Attachment 13: IND/IDE Documentation:** If submitting multiple documents, start each document on a new page. **Combine and upload as a single file named "IND-IDE.pdf."**
  - Complete the IND/IDE Documentation Form, which is available for download on the Full Announcement page for this Program Announcement/Funding Opportunity on Grants.gov.
  - If an IND or IDE application has been submitted, provide an explanation of the status of the IND or IDE application (e.g., past the critical 30-day period, pending response to questions raised by the Agency, on clinical hold). Provide a summary of previous meetings with the FDA on development of this product, if appropriate. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.
  - If the IND or IDE application is not yet submitted, provide evidence that an IND or IDE will be submitted within 60 days of award. Examples include results and minutes of a pre-IND or pre-IDE meeting with the FDA, a pre-IND/pre-IDE meeting request to the FDA, or other communication with the FDA. Provide the anticipated date of IND/IDE submission.
  - If an IND or IDE is not required for the proposed study, provide evidence in the form of communication from the FDA or the IRB of record to that effect.

- **Attachment 14: Collaborating DoD Military Facility Budget Form(s), if applicable: Upload as "MFBudget.pdf."** If a Military Facility (military health system facility, research laboratory, treatment facility, dental treatment facility, or a DoD activity embedded with a civilian medical center) will be a collaborator in performance of the project, complete the Collaborating DoD Military Facility Budget Form (available for download on the eBRAP "Funding Opportunities & Forms" web page), including a budget justification, for each Military Facility as instructed. Refer to the General Application Instructions, Section II.C.8., for detailed information.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C.4., for detailed information.
   - PI Biographical Sketch (five-page limit): Upload as "Biosketch_LastName.pdf." The suggested biographical sketch format is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP. The five-page National Institutes of Health Biographical Sketch may also be used.

- PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
- Key Personnel Biographical Sketches (five-page limit each): Upload as "Biosketch_LastName.pdf."
- Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C.5., for detailed information.
   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf." 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.

5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C.6., for detailed information.

6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C.7., for detailed information.

D. Applicant Verification of Grants.gov Submission in eBRAP

Prior to the end of the application verification period, PIs and organizational representatives can review and modify in eBRAP certain components of an application submitted to Grants.gov. Following retrieval and processing of the Grants.gov application, eBRAP will notify the organizational representatives and PI by email to log into eBRAP to review, modify, and verify the Grants.gov application submission. eBRAP will validate retrieved files against the specific Program Announcement/Funding Opportunity requirements and discrepancies will be noted in both the email and in the Full Application Files tab in eBRAP. eBRAP does not confirm the accuracy of file content. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the Program Announcement/Funding Opportunity. ***If either the Project Narrative or the budget fails eBRAP validation, an updated Grants.gov application package must be submitted via Grants.gov as a "Changed/Corrected Application" with the previous Grants.gov Tracking ID prior to the application submission deadline.*** The Project Narrative and Budget Form cannot be changed after the application submission deadline.

E. Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet either of these deadlines will result in application rejection.

F. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a DUNS number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the SAM with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Section II.A., for information on Grants.gov registration requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the DHA RDA Directorate and the OASD(HA), based on (a) technical merit and (b) the relevance to the mission of the DHP and VRP, and to the specific intent of the award mechanism. The highest-scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a nondisclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from Federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Process

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are of decreasing order of importance:
    - **Research Strategy and Feasibility**
        - How well the scientific rationale for testing the intervention is supported by the preliminary data, critical review and analysis of the literature, and/or laboratory/preclinical evidence.

- How well the study aims, hypotheses or objectives, experimental design, methods, data collection procedures, and analyses are designed to answer clearly the clinical objective.
- How well the inclusion and randomization criteria meet the needs of the proposed clinical trial.
- How well the exclusion criteria are justified.
- How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.
- To what degree the data collection instruments (e.g., surveys, questionnaires), if applicable, are appropriate to the proposed study.
- How well potential challenges and alternative strategies are discussed.

- **Impact**
  - How well the proposed research project addresses one or more of the FY15/16 VRP CTA Capability Gaps and, if applicable, FY15/16 VRP CTA Focus Areas.
  - How the potential outcomes of the proposed clinical trial will provide short-term benefits for individuals.
  - How effective the proposed research project will be in making important contributions toward the goal of advancing vision research and/or patient care.
  - How well the proposed research project addresses a critical problem in vision research, patient care, and/or quality of life.
  - To what extent the practical application of the proposed intervention will have a long-term benefit in individuals living with visual dysfunction and impact patient care and/or quality of life.
  - To what degree the intervention represents an improvement over currently available interventions and/or standards of care.
- **Military Benefit**
  - How relevant the anticipated outcomes of the proposed research are to military Service members and Veterans recovering from military-relevant injuries and diseases incident to military service.
  - The potential immediate and/or long-term benefits of the proposed research on the health and well-being of Service members, Veterans, and/or their families or communities.
- **Statistical Plan**
  - To what degree the statistical model and data analysis plan are suitable for the planned study.
  - How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.

- Whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.

- **Personnel and Communication**
  - Whether the composition of the study team (e.g., study coordinator, statistician) is appropriate.
  - To what degree the study team's background and expertise are appropriate to accomplish the proposed work (e.g., statistical expertise, expertise in the disease, and clinical studies).
  - How the levels of effort of the study team members are appropriate for successful conduct of the proposed trial.
  - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.
- **Intervention**
  - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
  - To what degree the intervention addresses the clinical need(s) described.
  - To what degree the PI has provided preclinical and/or clinical evidence to support the safety of the intervention.
  - Whether a member of the study team holds the IND/IDE for the indication proposed or whether the timeline proposed for obtaining the IND/IDE is appropriate (if applicable).
  - For investigator-sponsored INDs, whether there is evidence of appropriate institutional support, including capabilities to ensure monitoring as required by the FDA.
  - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.
  - Whether measures are described to ensure the consistency of dosing of active ingredients for nutritional supplements (if applicable).
- **Recruitment, Accrual, and Feasibility**
  - How well the PI addresses the availability of human subjects for the clinical trial and the prospect of their participation.
  - Whether the PI has demonstrated access to the proposed human subjects population.
  - The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
  - How well the application identifies possible delays (e.g., slow accrual, attrition) and presents adequate contingency plans to resolve them.

- To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study (e.g., Will human subjects still be able to take their regular medications while participating in the clinical trial? Are human subjects required to stay overnight in a hospital?)

- **Transition Plan**
  - Whether the funding strategy described to bring the outcome(s) to the next level of development (e.g., higher phase clinical trial, transition to industry, delivery to the market, incorporation into standard practice) is appropriate.
  - How the development plan to support a product label change, if applicable, is appropriate and well described.
  - Whether appropriate collaborations and other resources for providing continuity of development are established and/or well described.
  - How the schedule and milestones for bringing the outcome(s) to the next level of development (e.g., higher phase clinical trial, transition to industry, delivery to the market, incorporation into standard practice) are appropriate.
  - How well the potential risk analysis for cost, schedule, manufacturability, and sustainability is developed.
  - How well the application identifies intellectual property ownership, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any potential impact of intellectual property issues on product development and subsequent Government access to products supported by this Program Announcement/Funding Opportunity.
  - For knowledge products, to what degree the transition includes appropriate strategies for further knowledge development, dissemination, and incorporation into clinical care.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Environment**
  - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
  - To what degree the quality and extent of institutional support/commitment are appropriate for the proposed research project.

- **Ethical Considerations**
  - How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
  - How well the evidence shows that the procedures are consistent with sound research design and, when appropriate, that these procedures are already in use for diagnostic or treatment purposes.

- To what degree privacy issues are appropriately considered.
- To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Budget**
  - Whether the budget is appropriate for the proposed research and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influence the review.

2. **Programmatic Review:** To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following equally considered criteria are used by programmatic reviewers:

   a. Ratings and evaluations of the peer reviewers

   b. Relevance to the mission of the DHP and FY15/16 VRP, as evidenced by the following:
   - Adherence to the intent of the award mechanism
   - Program portfolio composition
   - Relative impact and military relevance

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive email notification of posting of the funding recommendation in eBRAP. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from eBRAP or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the application:

- Pre-application (Letter of Intent) was not submitted.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Human Subject Recruitment and Safety Procedures (Attachment 6) is missing.
- Intervention (Attachment 7) is missing.
- Data Management (Attachment 8) is missing.

B. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.

C. Withdrawal

The following may result in administrative withdrawal of the application:

- A FY15/16 VRP IP member is named as being involved in the research proposed or is 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 documentation. **A list of the FY15/16 VRP IP members can be found at http://cdmrp.army.mil/vrp/panels/panels15.**
- The application fails to conform to this Program Announcement/Funding Opportunity description to the extent that appropriate review cannot be conducted.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- An application submitted by a PI who does not meet the eligibility criteria will be withdrawn.
- The proposed research is not a clinical trial.

- If the application does not address at least one of the FY15/16 VRP Capability Gaps, the application will be withdrawn.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards made with FY15 funding will be made no later than September 30, 2016. Awards made with FY16 funding will be made no later than September 30, 2017. Refer to the General Application Instructions, Appendix 3, for additional award administration information.

Any assistance instrument awarded under this Program Announcement/Funding Opportunity will be governed by the award terms and conditions, which conform to DoD's implementation of the Office of Management and Budget (OMB) circulars applicable to financial assistance. Terms and conditions of new awards made after December 26, 2014 may include revisions to reflect DoD implementation of new OMB guidance in the Code of Federal Regulations, Title 2, Part 200, "Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards" (2 CFR part 200).

B. Administrative Requirements

Refer to the General Application Instructions, Appendix 3, for general information regarding administrative requirements.

C. National Policy Requirements

Refer to the General Application Instructions, Appendix 4, for general information regarding national policy requirements.

D. Reporting

Refer to the General Application Instructions, Appendix 3, Section I, for general information on reporting requirements. Quarterly technical progress reports and quad charts will be required. In addition to written progress reports, in-person presentations may be requested.

E. Award Transfers

The institution transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer.

Refer to the General Application Instructions, Appendix 3, Section M, for general information on organization or PI changes.

VI. AGENCY CONTACTS

A. 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 eBRAP should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@eBRAP.org

B. Grants.gov Contact Center

Questions related to application submission through 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). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 800-518-4726

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity or by responding to the prompt provided by Grants.gov when first downloading the Grants.gov application package. If the Grants.gov application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Upload Order	Action	Completed
SF-424 (R&R) Application for Federal Assistance		Complete form as instructed.	
Attachments Form	1	Project Narrative: Upload as Attachment 1 with file name "ProjectNarrative.pdf."	
	2	Supporting Documentation: Upload as Attachment 2 with file name "Support.pdf."	
	3	Technical Abstract: Upload as Attachment 3 with file name "TechAbs.pdf."	
	4	Lay Abstract: Upload as Attachment 4 with file name "LayAbs.pdf."	
	5	Statement of Work: Upload as Attachment 5 with file name "SOW.pdf."	
	6	Human Subject Recruitment and Safety Procedures: Upload as Attachment 6 with file name "HumSubProc.pdf."	
	7	Intervention: Upload as Attachment 7 with file name "Intervention.pdf."	
	8	Data Management: Upload as Attachment 8 with file name "Data_Manage.pdf."	
	9	Study Personnel and Organization: Upload as Attachment 9 with file name "Personnel.pdf."	
	10	Surveys, Questionnaires, and Other Data Collection Instructions: Upload as Attachment 10 with file name "Surveys.pdf."	
	11	Impact and Military Benefit Statement: Upload as Attachment 11 with file name "ImpactMilBen.pdf."	
	12	Transition Plan: Upload as Attachment 12 with file name "Transition.pdf."	
	13	IND/IDE Documentation: Upload as Attachment 13 with file name "IND-IDE.pdf."	
	14	Collaborating DoD Military Facility Budget Form(s): Upload as Attachment 14 with file name "MFBudget.pdf," if applicable.	
Research & Related Senior/Key Person Profile (Expanded)		Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.	
		Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.	
		Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.	
		Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person to the appropriate field.	

Grants.gov Application Components	Upload Order	Action	Completed
Research & Related Budget		Complete as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.	
Project/Performance Site Location(s) Form		Complete form as instructed.	
R & R Subaward Budget Attachment(s) Form		Complete form as instructed.	
Additional Application Components	**Upload Order**	**Action**	**Completed**
Confidential Letters of Recommendation		Confirm upload to eBRAP.	