Program Announcement

I. GENERAL INFORMATION

This program announcement is being released before the receipt of Federal funds appropriated in a bill for this program; funding of proposals received in response to this program announcement is contingent on the receipt of these funds at the United States Army Medical Research and Materiel Command (USAMRMC).

A. Title of Award: ***Neurofibromatosis Research Program (NFRP) Therapeutic Development Award.***

B. Program Name: Department of Defense (DOD) Fiscal Year 2006 (FY06) NFRP.

C. Funding Opportunity Number: W81XWH-06-NFRP-TDA.

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

E. Agency Contact(s)

1. Questions related to the program announcement, proposal format, or required documentation: Applicants should submit questions as early as possible. Every effort will be made to answer questions within 5 working days.

Phone:	301-619-7079
Fax:	301-619-7792
E-mail:	cdmrp.pa@amedd.army.mil
Mail:	Commander US Army Medical Research and Materiel Command ATTN: MCMR-ZB-C (NF06-TDA) 1077 Patchel Street (Building 1077) Fort Detrick, MD 21702-5024

2. Questions related to electronic submission: A help line for questions relating to proposal submission and the CDMRP eReceipt Online Proposal Submission System is available Monday through Friday from 8:00 a.m. to 5:00 p.m. Eastern time at 301-682-5507. Help also is available on the CDMRP website or by e-mail as follows:

Website:	https://cdmrp.org (User's Guide located in upper right corner of the proposal submission website)
E-mail:	help@cdmrp.org

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

Fax:	301-619-2937
E-mail:	qa.baa@amedd.army.mil
Mail:	Director US Army Medical Research Acquisition Activity ATTN: MCMR-AAA-R 820 Chandler Street Fort Detrick, MD 21702-5014

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

H. Website to Access Application Package: Proposals must be submitted at https://cdmrp.org. This website contains all the information, forms, documents, and links needed to apply. Applicants experiencing difficulty in downloading documents should contact the CDMRP as indicated in Subsection I.E.2.

I. Award/Regulatory Approval: The applicant may not use, employ, or subcontract for the use of any human subjects, human biological substances, cadavers, or laboratory animals until applicable regulatory documents are requested, reviewed, and approved by the USAMRMC.

II. FUNDING OPPORTUNITY DESCRIPTION

A. Program History: The Therapeutic Development Award is one of the mechanisms of the Neurofibromatosis Research Program (NFRP), which was established in FY96 to promote research directed toward decreasing the impact of neurofibromatosis (NF). Appropriations for the NFRP from FY96 through FY05 totaled $155.3 million (M). During this time, 24 Therapeutic Development Award proposals have been received and 9 have been funded. The FY06 appropriation is $17M.

B. Program Objectives: The overall goal of the FY06 NFRP is to develop effective therapies for NF1, NF2, and Schwannomatosis. Within this context, support for the training of NF researchers, the encouragement of established scientists in the field, and the attraction of new scientific expertise from other fields is essential to the NF community. Proposals to the NFRP are sought across all areas of laboratory, clinical, behavioral, and epidemiological research including all disciplines within the basic, clinical, psychosocial, behavioral, sociocultural, and environmental sciences, nursing, occupational health, alternative therapies, public health and policy, and economics. Additionally, proposals that address the needs of minority, low-income, rural, and other underrepresented and/or medically underserved populations are encouraged and may be submitted from any eligible institutional source.

C. Award Mechanism Description: The intent of the Therapeutic Development Award is to sponsor the development of therapeutics and the tools for their evaluation in preclinical model systems of NF1, NF2, and/or Schwannomatosis. The overall goal of this award mechanism is to accelerate the introduction of improved therapies for NF and Schwannomatosis into the clinical setting by supporting (1) the development of tools or platforms (including animal models) to identify lead agents or assess preclinical efficacy, and/or (2) the generation of the preclinical data necessary to conduct clinical trials after completion of the proposed research. The proposed studies are expected to be empirical in nature and product-driven, but may have a hypothesis-driven approach provided the focus is on therapeutics.

Please note that the Therapeutic Development Award mechanism is designed to support the development of tools, platforms, and model systems to be used for ***preclinical testing of therapeutics*** for NF and/or Schwannomatosis. Investigators interested in developing and/or validating tools, platforms, or model systems for ***basic research*** (i.e., not for therapeutic studies) should apply instead to the NFRP FY06 Resource Development Award .

Therapeutic Development Award proposals are limited to the areas of programmatic interest listed below. Proposals must focus on one or more of these areas to be considered for funding. Proposals that do not focus on at least one of the following areas will be administratively withdrawn.

- Development and/or validation of high-throughput screens or models to aid in defining targets with therapeutic potential
- Identification of novel therapeutics or lead agents through screening of libraries of small molecule compounds
- Development, modification, and/or validation of preclinical model systems for the pharmacological and/or pharmacokinetic testing of lead compounds and potential therapeutics
- Evaluation of novel and/or existing therapeutic modalities using established or validated novel preclinical model systems of NF1, NF2, and/or Schwannomatosis;

Proposals must include ***preliminary data*** relevant to the phase(s) of the preclinical development process covered by the research in their proposals. If appropriate, the proposal should include a clear statistical plan of analysis.

The NFRP is particularly interested in developing coordinated, multidisciplinary, goal/product-driven consortia focused on the development of therapeutics for NF1, NF2, and/or Schwannomatosis. Consortia should be dedicated to a single, synergistic preclinical development project or study rather than an additive set of subprojects (i.e., the combined efforts of the whole consortium provide greater benefit than the sum of individual research initiatives). Each consortium should comprise a multidisciplinary and multi-institutional research team of scientists and/or clinicians who have made significant contributions or have specific expertise related to the central theme of the proposal. If a consortium is proposed, sufficient characterization of the consortium and justification for the collaborative partners must be included in the proposal. ***Letters confirming/supporting collaboration are required.***

Participating institutions must be willing to resolve potential intellectual and material property issues and to remove institutional barriers that might interfere with achieving high levels of cooperation to ensure the successful establishment and maintenance of the consortia. An intellectual and material property plan is required as part of the supporting documentation of this proposal (see Subsection V.L).

Biotechnology and pharmaceutical companies are encouraged to apply for this award mechanism. If a biotechnology or pharmaceutical company applies for this mechanism as an individual submitter or as part of a consortium (see below), the company is expected to leverage its own resources to complement the funding provided for the study by this award.

III. AWARD INFORMATION

Although there are no total dollar amount restrictions to these awards, programmatic priority will be given to smaller-scale, cost-efficient projects with well-defined endpoints. Additionally, to foster the development of collaborative preclinical research teams, programmatic priority will be given to studies conducted by multidisciplinary, multi-institutional consortia.

Funding can be requested for up to 3 years. Direct costs can cover salary, expenses including research supplies, equipment, and travel to scientific/technical meetings. Indirect costs should be added as appropriate. If a biotechnology or pharmaceutical company applies for this mechanism as an individual submitter or as part of a consortium, the company is expected to leverage its own resources to complement the funding provided for the study by this award. For proposals involving a consortium, direct costs also can cover expenses for meetings that bring together members of the consortium.

The nature of the NFRP does not allow for renewal of grants or supplementation of existing grants.

The CDMRP expects to allot approximately $4M of the $17M FY06 NFRP appropriation to fund approximately one or two Therapeutic Development Awards, depending on the quality and number of proposals received.

IV. ELIGIBILITY INFORMATION

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

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

To protect the public interest, the Federal Government ensures the integrity of Federal programs by only conducting business with responsible recipients. The USAMRMC uses the Excluded Parties List System (EPLS) to exclude recipients ineligible to receive Federal awards. The EPLS

is online at http://epls.arnet.gov. (Reference Department of Defense Grant and Agreement Regulations (DODGAR) 25.110.)

B. Institutions: Eligible institutions include for-profit, nonprofit, public, and private organizations, such as universities, colleges, hospitals, laboratories, and companies. The USAMRMC is especially interested in receiving applications from Historically Black Colleges and Universities/Minority Institutions (HBCU/MI).

A DOD goal is to allocate funds for the CDMRP peer reviewed research to fund proposals from HBCU/MI. This provision is based on guidance from Executive Orders.[1] Proposals are assigned HBCU/MI status when the submitting institution is so designated by the Department of Education on the date the program announcement is released. The most current Department of Education list is posted on the CDMRP website at http://cdmrp.army.mil/spp under "Minority Institutions."

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

Proposals from Federal agencies ***must*** provide a plan delineating how all funds will be obligated by September 30, 2007, and how funds will be available to cover research costs over the entire award period. The plan must include the funding mechanism(s) that will be used to carry over funds between fiscal years, such as administrative agreements with foundations, non-Federal institutions, and universities.

C. Duplicate Submissions: Submission of the same research project to different FY06 NFRP award mechanisms or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative proposals.

V. PROPOSAL PREPARATION AND SUBMISSION INFORMATION

A. Proposal Components Summary: This subsection is a summary of submission requirements. Details, URLs, and other links are provided in the appropriate subsections of this program announcement. Proposals will be evaluated according to peer and programmatic review criteria in Section VI.

1. Applicant Responsibility: The applicant is responsible for entering and/or uploading the following information into the CDMRP eReceipt Online Proposal Submission System at https://cdmrp.org:

[1]Executive Orders 12876, 12900, and 13021

Item	Tab	Format	Action
Letter of Intent (LOI)	Proposal Information	Typed	Copy the LOI into the data field. Click the "Save and Forward Letter of Intent" button to automatically create the LOI.
Proposal Information	Proposal Information	Typed	Enter the appropriate information in data fields.
Proposal Contacts	Proposal Contacts	Typed	Enter contact information for the applicant and the Contract Representative at the applicant's institution.
Collaborators and Conflicts of Interest (COI)	Collaborator/COI	Typed	Enter information about collaborators and others outside the scope of the proposal who may have a COI in the review of this proposal.
Proposal Abstracts, Impact Statement, and Statement of Work (SOW)	Abstract/Impact/ SOW	Typed or Cut and Paste	Enter the Technical Abstract, Public Abstract, Impact Statement, and SOW in separate data fields.
Proposal Main Body	Required Files	PDF	Upload as a PDF file.
Supporting Documentation	Required Files	PDF	Upload as a PDF file.
Budget Information	Required Files	PDF	Upload as a PDF file.
Regulatory Documents	Required Files	PDF	Upload the Certificate of Environmental Compliance and the Principal Investigator Safety Program Assurance forms.

2. Contract Representative Responsibility: The Contract Representative (CR) or institutional official responsible for sponsored program administration (or equivalent) at the applicant's institution is responsible for the following:

Item	Tab	Format	Action
Contract Representative's Contact Information Profile	My Profile for the CR	Typed	Complete before electronic approval of all submission components

Item	Tab	Format	Action
USAMRAA[a]-Required Documents	My Profile for the CR	PDF	Upload the Rate Agreement, Certifications and Assurances for Assistance Agreements, and Representations for Assistance Agreements.
Approval	CR Approval	Click Approval Button	Click the button to approve the Proposal Information, Proposal Contacts, Collaborators and COI, Abstracts/Impact Statement/SOW, and Required Files ***before*** the submission deadline of 5:00 p.m. Eastern time, April 25, 2006.

[a]US Army Medical Research Acquisition Activity

B. Proposal Format: Proposals must be uploaded under the "Required Files" tab of the CDMRP eReceipt Online Proposal Submission System at https://cdmrp.org. Applicants unfamiliar with the preparation of PDF files are encouraged to acquire and learn to use the appropriate software well in advance of the submission deadline. The instructions in this subsection must be followed carefully to prepare proposals for PDF submission.

The main body of the proposal must be clear and legible and conform to the formatting guidelines described below. The font size, spacing, page size, and margins may differ between the word processing, PDF, and printed versions. These guidelines apply to the document properties of the electronic version of the PDF file(s) as viewed on the computer screen and submitted via the CDMRP eReceipt Online Proposal Submission System.

- **Font Size:** 12 point or larger.
- **Font Type:** Times New Roman is strongly recommended.
- **Spacing:** No more than six lines of type within a vertical inch (2.54 cm).
- **Page Size:** No larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- **Margins:** Must be at least 0.5 inch (1.27 cm) in all directions.
- **Print Area:** 7.5 inches x 10.0 inches (approximately 19.05 cm x 25.40 cm).
- **Color, High-Resolution, and Multimedia Objects:** Proposals may include color, high-resolution, or multimedia objects (e.g., MPEG, WAV, or AVI files) embedded in the PDF files; however, these objects must not exceed 15 seconds in length and a size of 10 MB. Since some reviewers work from black and white printed copies, applicants may wish to include text in the proposal directing the reviewer to the electronic file for parts of the proposal that may be difficult to interpret when printed in black and white. Photographs and illustrations must be submitted in JPEG format; bit map or TIFF formats are not allowed.

- **Internet URLs:** URLs directing reviewers to websites containing significant additional information about the proposed research are not allowed in the proposal or its components. Inclusion of such URLs may be perceived as an attempt to gain an unfair competitive advantage. Links to publications referenced in the proposal are allowed.
- **Language:** English.

Please note that headers should not be included, as the proposal log number will be electronically captured on each page of the proposal after receipt.

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

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

- Proposal body exceeds page limit.
- Proposal body is missing.
- Detailed cost estimate is missing.
- Proposal is incomplete after the deadline.
- Proposal does not address one of the FY06 NFRP programmatic interests (development and/or validation of high-throughput screens or models; identification of lead agents through screening of small molecule libraries; development, modification, and/or validation of preclinical models; or evaluation of novel and/or existing therapeutic modalities in preclinical model systems).

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

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

The electronic PDF file uploaded in the CDMRP eReceipt Online Proposal Submission System is the official proposal submission file. After conversion of word processing documents to PDF files and before electronic submission, applicants should review their files to ensure that the proposal complies with the preparation guidelines outlined in this program announcement.

D. Letter of Intent (LOI): An LOI (a brief description of the proposal) is entered in a data field under "My Proposals: Create New Proposal". The LOI is saved when the "Save and Forward Letter of Intent" button is selected. The LOI may be modified under "Proposal Information" at anytime before the applicant submits this information by clicking "Finalize for CR Approval." The LOI should be submitted by ***March 28, 2006*** at https://cdmrp.org.

E. Proposal Information: Applicants are required to submit the Proposal Information as described in https://cdmrp.org before uploading the proposal, supporting documentation, and budget information.

- A ***Title/Referral Page*** for the proposal will be generated from the information uploaded in eReceipt and appended to the proposal electronically by the CDMRP eReceipt system.

F. Proposal Contacts: The Proposal Contacts ***must*** include the e-mail address of a Contract Representative authorized to negotiate on behalf of the applicant's institution. The Proposal Contacts must be approved by the Contract Representative at the applicant's institution.

G. Collaborators and Conflicts of Interest (COI): To avoid COI during the review process, list the names of all scientific participants in the proposal including collaborators, consultants, and subawardees. In addition, list the names of individuals outside the scope of this proposal who may have a COI in reviewing this proposal.

H. Proposal Abstracts – 5,700-character limit including spaces (approximately one page), for each abstract: Each abstract must include the applicant's name and the title of the proposal. A structured technical abstract and a public (nontechnical) abstract are required. These abstracts are vitally important in both the peer review and programmatic review processes. Programmatic review is based on the Integration Panel's review of these two abstracts as part of the peer review summary statements; therefore, it is of paramount importance that the applicant submit abstracts that describe the proposed work fully. Each abstract must be entered into the appropriate data field under the "Abstract/Impact/SOW" tab of the CDMRP eReceipt system.

Applicants can type the abstracts or "cut and paste" them from a word processing application into the respective data fields. ***Spell out all Greek letters, other non-English letters, and symbols.***

Abstracts of all funded proposals will be posted on the CDMRP website at http://cdmrp.army.mil. Proprietary or confidential information should ***not*** be included in either the technical or the public abstract.

1. Technical Abstract: Sample technical abstracts can be found at http://cdmrp.org/samples.cfm. The structured technical abstract must provide a clear and concise overview of the proposed work. Use the outline below when preparing the structured technical abstract.

- Background: Present the ideas and reasoning behind the proposed work.
- Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
- Specific Aims: State the specific aims of the study.
- Study Design: Briefly describe the study design including appropriate controls.

- Impact: Provide a brief statement explaining the impact of the proposed work to program goals. Describe how the proposed project will have an impact on the treatment of NF1, NF2, and/or Schwannomatosis.

2. Public Abstract: Sample public abstracts can be found at http://cdmrp.org/samples.cfm. The public abstract is intended to communicate the purpose and rationale of the study to a non-scientifically trained audience. The public abstract is an important component of the proposal review process because consumer advocates, who are part of the review and funding decision process, use this abstract as a part of their review.

- Describe the scientific objective and rationale for the proposal in a manner readily understood by non-scientists.
  - Do not duplicate the technical abstract.
- Describe the ultimate applicability of the research.
  - What types of patients will it help and how will it help them?
  - What are the potential clinical applications, benefits, and risks?
  - What is the projected time it may take to achieve a consumer-related outcome?
- If the research is too basic for clinical applicability, describe the interim outcomes.
  - What types of contributions will this study make to advance research?
  - How will the research enhance this or other studies being conducted?

I. Impact Statement – 5,700-character limit including spaces (approximately one page): The Impact Statement is captured as a data field under the "Abstract/Impact/SOW" tab in the CDMRP eReceipt system. Applicants can type the Impact Statement into the data field or "cut and paste" it from a word processing application.

State explicitly how the proposed work will make an original and important contribution to the NF and/or Schwannomatosis research fields**.** Describe the impact of this study on the concepts and methods that drive the field(s) and or the impact on the treatment of NF and/or Schwannomatosis. Explain the potential clinical applications, benefits, and risks. The Impact Statement, which will be available at both peer and programmatic reviews, is often cited by consumer advocates during the review and funding decision processes.

J. Statement of Work – 11,400-character limit including spaces (approximately two pages): The SOW is captured as a data field under the "Abstract/Impact/SOW" tab in the CDMRP eReceipt system. Applicants can type in the SOW into the data field or "cut and paste" it from a word processing application.

The SOW is a concise restatement of the research proposal that outlines, step by step, how each major goal or objective of the proposed research/services will be accomplished during the period for which the USAMRMC will provide financial support. When a proposal requesting funding as part of a larger study is submitted, the proposal's SOW must include DOD-funded tasks only. Sample SOWs can be found at http://cdmrp.org/samples.cfm .

The SOW should:

- Describe the work to be accomplished as tasks (tasks may relate to specific aims);
- Identify the timeline and milestones for the work over the performance period for the proposed effort;
    - Allow 4 to 6 months for regulatory review and approval processes for human use studies;
    - Allow 2 months for regulatory review and approval processes for animal studies;
- For animal and human studies (including tissue, anatomical, or biological substances), indicate the sample size projected or required for each task;
- Identify methods; and
- Identify outcomes, products, and deliverables for each phase of the project.

K. Proposal Main Body: Start section on a new page; 25-page limit inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other information needed to judge the proposal.

The proposal main body is uploaded as a PDF file under the "Required Files" tab of the CDMRP eReceipt system.

The inclusion of preliminary data is ***required*** for all Therapeutic Development Award proposal submissions. Investigators must submit promising and well-founded preliminary data relevant to NF/Schwannomatosis and the proposed project. ***The formation of synergistic, multidisciplinary, multi-institutional consortia is strongly encouraged.*** If a consortium is proposed, investigators must include sufficient characterization of the consortium and justification for the collaborative partners.

Describe the proposed project using the following outline:

1. Background: Present the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to this proposal. Cite relevant literature.

2. Hypothesis or Objective: State the hypothesis to be tested or the objective to be reached.

3. Specific Aims: Concisely explain the project's specific aims. If this proposal is part of a larger study, present only DOD-funded tasks.

4. Research Strategy: Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches. If human subjects or human biological samples will be used, include a detailed plan for the recruitment of subjects or the acquisition of samples.

5. Product: Describe the predicted or proposed product, its utility in the field, and its impact on NF1, NF2, and/or Schwannomatosis. Refer to specific programmatic interests listed in Subsection II.C.

6. Impact: The rationale should clearly reflect that the research is focused on results that will have a significant impact on the concepts or methods that drive the field and make an original and important contribution to the goal of advancing research on the treatment of NF and/or Schwannomatosis.

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

Supporting Documentation must be uploaded as a single PDF file under the "Required Files" tab of the CDMRP eReceipt system. All documents or letters that require signatures must be signed and incorporated into the supporting documentation file before it is submitted.

The first item in the Supporting Documentation file is the ***Checklist/Table of Contents page***. The requested, allowable items in this section must be listed in the Checklist/Table of Contents; these include:

1. Abbreviations: Start section on a new page; one-page limit. Provide a list of all acronyms, abbreviations, and symbols used in the main body of the proposal.

2. References: Start section on a new page; no page limit. List all relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

3. Biographical Sketches: Four-page limit per individual. Include biographical sketches for all key personnel including collaborating investigators and support staff. These documents are a critical component of the review process. Incomplete or missing biographical sketches may result in lower proposal scores. The Biographical Sketch form may be used. Use of this form is not mandatory, but the information requested shall be presented in a similar format.

4. Existing/Pending Support: Start section on a new page; no page limit. List the titles, time commitments, supporting agencies, durations, and levels of funding for all existing and pending research projects involving the applicant and key personnel on a separate page. If no support exists, enter "None." Proposals submitted under this program announcement should not duplicate other funded research projects.

5. Facilities/Equipment Description: No page limit. Describe the facilities available for performing the proposed research/services. Describe the institutional commitment, including any additional facilities or equipment proposed for purchase or available for use at no cost to the USAMRMC. Indicate whether Government-owned facilities or equipment are proposed for use.

6. Letters of Support: Provide letters of support from collaborating individuals or institutions.

7. Publications and/or Patent Abstracts: Five-document limit. Include up to five relevant publication reprints and/or patent abstracts. A patent abstract should provide a non-proprietary description of the patent application. If more than five publications are included in the submission, the extra items will not be peer reviewed.

8. Intellectual and Material Property Plan: No page limit. Provide a plan for resolving intellectual and material property issues among participating institutions.

M. Budget Information: Applicants must complete the Detailed Cost Estimate form and the Budget Justification form, and upload them as a single PDF file under the "Required Files" tab of the CDMRP eReceipt system. When a proposal requesting funding as part of a larger study is submitted, the proposal's budget justification should include only DOD-funded tasks.

1. Funding Restrictions: Although there are no total dollar amount restrictions to these awards, programmatic priority will be given to smaller-scale, cost-efficient projects with well-defined endpoints. The performance period can be requested for up to 3 years. Indirect costs should be added as appropriate. Direct costs can cover salary, expenses including research supplies, equipment, and travel to scientific/technical meetings. The amount for travel to scientific/technical meetings may not exceed $1,800 per year per investigator. Travel costs to bring collaborators or consortium members together are not included in this $1,800 per year per investigator limit but must be separately budgeted and fully justified. If a biotechnology or pharmaceutical company applies for this mechanism as an individual submitter or as part of a consortium, the company is expected to leverage its own resources to complement the funding provided for the study by this award.

2. Detailed Cost Estimate Form and the Budget Justification Instructions: Budget is an important consideration in both peer review and programmatic review, and applicants are cautioned to use discretion in budget requests. Budgets also will be reviewed during award negotiations. ***Organizations must provide sufficient detail and budget justification so that the Government can determine the proposed costs to be allocable and reasonable for the proposed research.*** All costs must be entered in U.S. dollars.

The USAMRMC encourages in-kind contributions and cost-sharing for CDMRP-supported research. In-kind contributions may include support of services (e.g., laboratory services and salaries of personnel), real property and equipment, and/or supplies (e.g., drugs, devices, reagents) directly benefiting and specifically identifiable to the research project. ***It is***

expected that institutions will share the cost of equipment purchased for this research proposal. Please see full details under "Major Equipment" in Subsection V.M.2.c.

Costs proposed must conform to the following regulations and principles:

- **Commercial Firms:** Federal Acquisition Regulations (FAR) Part 31 and Defense FAR Supplement Part 31 (http://farsite.hill.af.mil), Contract Cost Principles and Procedures.
- **Educational Institutions:** Office of Management and Budget (OMB) Circular A-21, Cost Principles for Educational Institutions (http://www.whitehouse.gov/omb/grants/grants_circulars.html).
- **Nonprofit Organizations:** OMB Circular A-122, Cost Principles for Nonprofit Organizations. OMB Circular A-133, Audits of Institutions of Higher Education and Other Nonprofit Organizations (http://www.whitehouse.gov/omb/grants/grants_circulars.html).
- **State, Local, and Tribal Governments:** OMB Circular A-87, Cost Principles for State, Local, and Indian Tribal Governments (http://www.whitehouse.gov/omb/grants/grants_circulars.html).

Follow the instructions below when providing the information requested in the Detailed Cost Estimate form.

a. Personnel

i. Name: Beginning with the applicant, list all participants who will be involved in the project during the initial budget period, whether or not salaries are requested. Include all collaborating investigators, research associates, individuals in training, and support staff. ***The applicant must be identified as the Principal Investigator of the proposal.***

ii. Role on Project: Identify the role of each participant listed. Describe his or her specific functions in the Budget Justification section of the Detailed Cost Estimate form.

iii. Type of Appointment (Months): List the number of months per year reflected in an individual's contractual appointment with the applicant organization. The Government assumes that appointments at the applicant organization are full time for each individual. If an appointment is less than full time, e.g., 50%, note this with an asterisk (*) and provide a full explanation in the Budget Justification section of the Detailed Cost Estimate form. Individuals may have split appointments (e.g., for an academic period and a summer period). For each type of appointment, identify and enter the number of months on separate lines.

iv. Annual Base Salary: Enter the annual institutional base salary for each individual listed for the project.

v. Percentage of Effort on Project: The applicant's qualifications and the amount of time that he or she and other professional personnel will devote to the research are important factors in selecting research proposals for funding. List the percentage of each appointment to be spent on this project for each key staff member. Include the percent effort of all unpaid collaborators and consultants.

vi. Salaries Requested: Enter the salaries in whole U.S. dollars for each position for which funds are requested. Calculate the salary request by multiplying an individual's institutional base salary by the percentage of effort on the project.

vii. Fringe Benefits: Fringe benefits for each position may be requested in accordance with institutional guidelines, provided the costs for all sponsors are treated consistently by the applicant's organization. Provide documentation to support the fringe benefits.

viii. Totals: Calculate the totals for each position and enter these as subtotals in the columns indicated.

b. Consultant Costs: Provide the names and organizational affiliations of all consultants whether or not funds are requested.

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

i. If the purchase of equipment for this research project is requested, it is expected that the applicant's institution will share 50% of the cost.

ii. Permanent equipment is any article of nonexpendable tangible property having a useful life of 2 years or longer and an acquisition cost of $5,000 or more per unit.

iii. The basis for the cost of each item of permanent equipment included in the budget must be disclosed.

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

d. Materials, Supplies, and Consumables: A general description and estimated total cost of expendable equipment and supplies are required. Itemize supplies in separate categories (e.g., glassware, chemicals, radioisotopes). Categories in amounts less than $1,000 do not need to be itemized. If animals will be purchased, state the species, strain

(if applicable), and the number of animals to be used. If human cell lines are to be purchased, state the source and the description.

e. Travel Costs: Costs for travel to scientific/technical meetings may not exceed $1,800 per year.

Travel costs associated with the execution of the proposed work should be entered in this section. If applicable, reasonable costs for travel between collaborating institutions should be included and are not subject to the yearly $1,800 limitation on travel to meetings. Justification for these travel costs should be provided. Travel outside the U.S. requires prior approval from the US Army Medical Research Acquisition Activity (USAMRAA).

f. Research-Related Subject Costs: Itemize costs of subject participation in the research study. These costs are strictly limited to expenses associated specifically with the proposed study. The USAMRMC will not provide funds for ongoing medical care costs not related to a subject's participation in the research study.

g. Other Direct Costs: Itemize other anticipated direct costs such as publication and report costs, rental for computers and other equipment (provide hours and rates), and communication costs. Unusual or expensive items should be fully explained and justified. Estimate the costs of publishing and reporting research results, including direct charges for clerical preparation, illustrations, reprints, and distribution.

h. Subaward Costs: A description of services or materials to be awarded by subcontract or subgrant is required. For awards totaling $10,000 or more:

- Identify the type of award to be used (e.g., cost reimbursement, fixed price);
- Identify the proposed subcontractor or subgrantee, if known, and provide an explanation of why and how the subcontractor or subgrantee was selected or will be selected;
- Specify whether the award will be competitive and, if noncompetitive, provide a rationale to justify the absence of competition; and
- Provide the proposed acquisition price.

i. Indirect Costs (overhead, general and administrative, and other): The most recent rates, dates of negotiation, base(s), and periods to which the rates apply should be disclosed with a statement identifying whether the proposed rates are provisional or fixed.

j. Total Costs for the Entire Proposed Period of Support (second page of the Detailed Cost Estimate form): Enter the totals in each budget category for all additional years of support requested and itemize these totals in the Budget Justification section of the Detailed Cost Estimate form. Note with an asterisk (*) and explain any significant increases or decreases from the initial year budget. All amounts should be in

U.S. dollars. Directs costs, indirect costs, and the total cost for the entire proposed period of support should equal the amount entered in the "Required Files" tab at https://cdmrp.org.

3. Budget Justification (third page of the Detailed Cost Estimate form): Each item in the budget must be clearly justified in the Budget Justification section of the Detailed Cost Estimate form.

4. Federal Agency Financial Requirement: Proposals from Federal agencies ***must*** provide a plan delineating how all funds will be obligated by September 30, 2007, and how funds will be available to cover research costs over the entire award period. The plan must include the funding mechanism(s), such as administrative agreements with foundations, non-Federal institutions, and universities.

Start the plan on a new page at the end of the Budget Information section. The Federal Agency Financial Plan must be uploaded as part of the budget information before the submission deadline of ***5:00 p.m. Eastern time, April 25, 2006***.

N. Regulatory Requirements: Completed and signed copies of the Certificate of Environmental Compliance and Principal Investigator Safety Program Assurance form must be uploaded under the "Required Files" tab of the CDMRP eReceipt system as separate PDF files.

Do not submit other regulatory documents (see Subsection VII.D.5, Research Involving Human Subjects/Biological Substances/Cadavers; see Subsection VII.D.4, Research Involving Animals) with the proposal. The applicant should provide these documents to the USAMRMC only upon request.

O. USAMRAA-Required Documents: The Contract Representative at the applicant's institution must upload the current version of the institution's negotiated Rate Agreement, the Certifications and Assurances for Assistance Agreements, and the Representations for Assistance Agreements. These documents must be uploaded as separate PDF files under the Contract Representative's "My Profile" tab of the CDMRP eReceipt system by the proposal submission deadline.

P. Submission Date and Time: Proposals must be approved on the CDMRP eReceipt system by the Contract Representative at the applicant's institution by the deadline. Proposals that are incomplete or not approved electronically before the deadline will not be considered for review. The eReceipt system will ***not*** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time, April 25, 2006 deadline.

The timeline for the Therapeutic Development Award is:

Online Letter of Intent:	Expected by ***March 28, 2006***
Online Proposal Information:	Required prior to proposal submission
Proposal Submission/Approval Deadline:	***5:00 p.m. Eastern time, April 25, 2006***
Peer Review (First Tier):	June 2006

Programmatic Review (Second Tier):	October 2006
Request for Additional Documents:	As early as 2 weeks after the completion of programmatic review
Notification Letter:	Approximately 4 weeks after the completion of programmatic review
Award Start Date:	Anticipated between December 2006 and April 2007

Q. Electronic Submission Requirements: Electronic submission is required. Only proposals submitted as PDF files through the CDMRP eReceipt system at https://cdmrp.org will be accepted.

Several steps are critical to successful proposal submission:

- The Proposal Information must be "Finalized for CR Approval" before the proposal is submitted. Applicants are encouraged to begin this part of the submission process early.
- Proposal Contacts must be "Finalized for CR Approval" before the proposal is submitted. The e-mail address of a Contract Representative at the applicant's institution must be included in the Proposal Contacts. Applicants are encouraged to begin this part of the submission process early.
- Applicants are encouraged to coordinate with their Contract Representative early in the application process.
- The Contract Representative authorized to negotiate on behalf of the applicant's institution is required to provide final approval before the proposal is accepted.
- The eReceipt system will ***not*** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time, April 25, 2006 deadline.
- Some items in the proposal including figures, tables, graphs, letters, or publications will need to be scanned electronically. These documents should be scanned at a resolution of 300 dpi or less.
- Applicants are encouraged to retain a date and time-stamped copy of the proposal component files as prepared by word processing software (e.g., Microsoft Word, WordPerfect) as well as the original PDF conversion file.
- The Detailed Cost Estimate form and the Budget Justification form must be uploaded under the "Required Files" tab of the CDMRP eReceipt system.
- The regulatory documents required at submission include a completed and signed Certificate of Environmental Compliance and a completed and signed Principal Investigator Safety Program Assurance form. These forms must be uploaded under the "Required Files" tab of the CDMRP eReceipt system.

VI. PROPOSAL REVIEW INFORMATION

A. Proposal Review and Selection Overview

1. Process: The CDMRP uses a two-tier review process for proposal evaluation. The two tiers differ fundamentally. The first tier is a scientific peer review of proposals against established criteria for determining scientific merit. The second tier is a programmatic review of proposals that compares submissions to each other and recommends proposals for funding based on scientific merit and overall goals of the program.

2. Peer Review: Peer review is conducted by scientific and consumer reviewers. The primary responsibility of the peer reviewers is to provide unbiased, expert advice on the scientific/technical merit and relevance of proposals based on the review criteria published for each award mechanism.

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

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

3. Programmatic Review: Programmatic review is conducted by the Integration Panel, which is composed of scientists, clinicians, and consumer advocates. The scientific members of the Integration Panel represent diverse disciplines and specialty areas, and the consumer members represent national advocacy constituencies. A function of programmatic review is to structure a broad portfolio of grants across all disciplines. Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool. Integration Panel members base programmatic review primarily on the peer review summary statements and the proposal abstracts. The Integration Panel also may review SOWs and impact statements. Full proposals are not forwarded to programmatic review.

HBCU/MI proposals are reviewed concurrently with others in the same research area during scientific peer review. However, they may be evaluated separately during programmatic review. Consistent with the CDMRP's goal, recommendations for funding HBCU/MI proposals are based on scientific excellence and program relevance.

B. Review Criteria

1. Peer Review: Therapeutic Development Award proposals will be evaluated by peer reviewers according to the following criteria. The reviewers will evaluate:

- **Research Strategy**
    - How the scientific rationale supports the feasibility and development of the proposed product as demonstrated by a critical review and analysis of the literature, preliminary data, and logical reasoning
    - How well the hypothesis or objectives, aims, experimental design, methods, and analyses are developed
    - How well the applicant acknowledges potential problems and addresses alternative approaches
    - Whether the study has clear product-driven endpoints
    - (As appropriate) The suitability of the screening assays and preclinical models to be developed, modified, and/or validated for identification and/or assessment of therapeutic agents
    - (As appropriate) Whether the applicant clearly demonstrates the intent to use the proposed tools or models for ***preclinical therapeutic testing*** (i.e., not for basic research)
    - (As appropriate) How the outlined chemical synthetic pathways for modification of lead compounds or the formulation of potential delivery systems are based in rational design
- **Relevance and Disease/Therapeutic Impact**
    - How the project addresses one or more of the programmatic interests (development and/or validation of high-throughput screens or models for NF and/or Schwannomatosis; identification of lead agents through screening of small molecule libraries; development, modification, and/or validation of preclinical models; or evaluation of novel and/or existing therapeutic modalities in preclinical model systems)
    - How the study makes an impact on the development of therapeutics for NF1, NF2, and/or Schwannomatosis
    - Whether models being developed, modified, and/or validated accurately reflect the molecular, cellular, and/or systemic biology of the disease(s)
    - For projects involving hypothesis-driven research, the impact on the concepts or methods that drive therapeutic development
- **Personnel**
    - Whether the applicant meets the eligibility requirements
    - How the research team's background and expertise are appropriate to develop the proposed product
    - Appropriateness of the levels of effort for successful development of the proposed product

- **For Proposals Involving Consortia**
  - Whether the consortium includes scientists and/or clinicians from at least two institutions.
  - Whether letters of collaboration are provided for any proposed collaborative arrangements

- **Environment**
  - The appropriateness of the scientific environment for the proposed research
  - How the research requirements are supported adequately by the availability of and accessibility to facilities and resources (including collaborative arrangements)
  - The quality and extent of institutional support
  - **For Proposals Involving Consortia**
    - The degree to which the consortium is goal-focused
    - Whether synergy exists between consortium members
    - Whether a clear plan for interaction between and among members exists
    - Effectiveness of plan for sharing and evaluating data in real time between and among members
    - How well the institutions/organizations involved in the project strengthen the proposal
    - Evidence of a plan to resolve intellectual and material property issues among participating institutions
- **Budget**
  - How the budget is appropriate for the proposed research
  - Appropriateness of distribution of funds among members of the consortium

2. Programmatic Review: Criteria used by the Integration Panel to make funding recommendations that maintain the NFRP's broad portfolio include:

- Ratings and evaluations of the peer reviewers (scientific and consumer),
- Programmatic relevance,
- Relative innovation and impact,
- Program portfolio balance, and
- Adherence to the intent of the award mechanism.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the Program are selected by the Integration Panel and recommended for funding to the Commanding General, USAMRMC.

VII. AWARD ADMINISTRATION INFORMATION

A. Award Notices: Each applicant will receive notification of the award status of his or her proposal. A copy of the peer review summary statement will be posted to the CDMRP eReceipt system. Applicants can expect to receive notification approximately four weeks after programmatic review.

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

Proposals from Federal agencies ***must*** provide a plan delineating how all funds will be obligated by September 30, 2007, and how funds will be available to cover research costs over the entire award period. The plan must include the funding mechanism(s) that will be used to carry over funds between fiscal years, such as administrative agreements with foundations, non-Federal institutions, and universities.

A change in institutional affiliation will require the investigator to resubmit the entire proposal packet through his or her new institution to include any regulatory documentation that may require protocols, etc. to be approved for the new institution. The investigator's original institution must agree to relinquish the award. Any delay in the submission of the new information will result in a delay in contracting, regulatory review, and a subsequent delay in resuming work on the project. ***Transferring an award that includes a Phase I, Phase II, or Phase III clinical trial will not be permitted.***

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

For multi-institutional studies, collaborating institutions must be willing to resolve potential intellectual and material property issues and remove institutional barriers to achieving high levels of cooperation to ensure the successful establishment and maintenance of the research project. An intellectual and material property plan agreed to by all participating institutions may be required during award negotiations.

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

D. Regulatory Review

1. Overview: Concurrent with the USAMRAA negotiation, the Office of Surety, Safety and Environment will review the Certificate of Environmental Compliance and the Principal Investigator Safety Program Assurance form submitted with the proposal. The applicable USAMRMC regulatory office will review documents related to research involving animal use, human subjects/anatomical substance use, and cadaver use submitted upon request to ensure that DOD regulations are met.

2. Certificate of Environmental Compliance: The Certificate of Environmental Compliance must be submitted with the proposal. If multiple research sites/institutions are funded in the proposal, then a Certificate of Environmental Compliance for each site will be requested at a later date.

3. Safety Program Documents: The Principal Investigator Safety Program Assurance form must be submitted with the proposal.

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

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

4. Research Involving Animal Use: Specific documents relating to the use of animals in the proposed research will be requested by the CDMRP if the proposal is selected for funding (these documents should not be submitted with the proposal). The Animal Care and Use Review Office (ACURO), a component of USAMRMC Office of Research Protections (formerly Regulatory Compliance and Quality), must review and approve all animal use prior to the start of working with animals. Applicants must complete and submit the animal use appendix titled "Research Involving Animals," which can be found on the ACURO website https://mrmc-www.army.mil/rodorpaurd.asp).

Questions related to animal use may be directed to ACURO as follows:

Phone:	301-619-6694
Fax:	301-619-4165
E-mail:	acuro@amedd.army.mil
Mail:	MCMR-ZB-PA 504 Scott Street Fort Detrick, MD 21702-5012

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

5. Research Involving Human Subjects/Biological Substances/Cadavers: In addition to local Institutional Review Board (IRB) approval to conduct research involving human subjects and/or human biological substances or cadavers, a second tier of IRB review and approval also is required by the DOD. This second review is conducted by the Human Subjects Research Review Board (HSRRB), which is administered by the USAMRMC Office of Research Protections. The HSRRB is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed and will require information in addition to that supplied to the local review board.

a. Requirements: Specific requirements for research involving human subjects, human biological substances, and/or cadavers can be found at https://mrmc.detrick.army.mil/docs/rcq/HumanSubjectsAppendix.pdf.

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

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

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

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

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

Furthermore and consistent with the Common Federal Policy for the Protection of Human Subjects, if an individual cannot give his or her own consent to participate in a research study, consent of the individual's legally authorized representative must be obtained before the individual's participation in the research. Moreover, an individual not legally competent to consent (e.g., incapacitated individuals, incompetents, minors) may not be enrolled in DOD-sponsored research unless the research is intended to benefit each subject enrolled in the study. For example, a subject may benefit directly from medical

treatment or surveillance beyond the standard of care. Investigators should be aware that this law makes placebo-controlled clinical trials problematic because of the "intent to benefit" requirement whenever participation is sought of subjects from whom consent must be obtained by the legally authorized representative.

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

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

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

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

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

6. Award/Regulatory Approval: The applicant may not use, employ, or subcontract for the use of any human subjects, human anatomical substances/cadavers, or laboratory animals without written approval from the applicable USAMRMC regulatory office once an award is made. The applicable USAMRMC regulatory office will forward written approvals directly to the applicant.

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

Reporting requirements include the following:

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

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

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

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

VIII. OTHER INFORMATION

A. Disclosure of Proprietary Information outside the Government: By submitting a proposal, the applicant understands that proprietary information 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 proposal will only be used for evaluation purposes and will not be further disclosed or used. Funded proposals may be subject to public release under the Freedom of Information Act; proposals that are not selected for funding are not subject to public release.

B. Government Obligation: Applicants are cautioned that only an appointed Contracting/Grants Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government to fund preparation of a proposal or to support research should be inferred from discussions with a technical project officer. Applicants who, or

organizations that, make financial or other commitments for a research effort in the absence of an actual legal obligation signed by the USAMRAA Contracting/Grants Officer do so at their own risk.

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

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

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

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

IX. ACRONYM LIST

AVI	Audio Video Interleave
CCR	Central Contractor Registration
CDMRP	Congressionally Directed Medical Research Programs
CFDA	Catalog of Federal Domestic Assistance
CFR	Code of Federal Regulations
COI	Conflict of Interest
CR	Contract Representative
DOD	Department of Defense
DODGAR	Department of Defense Grant and Agreement Regulations
EPLS	Excluded Parties List System
FAR	Federal Acquisition Regulations
FY	Fiscal Year
HBCU/MI	Historically Black Colleges and Universities/Minority Institutions
hES	Human Embryonic Stem
HSRRB	Human Subjects Research Review Board
IRB	Institutional Review Board
JPEG	Joint Photographic Experts Group
M	Million
MPEG	Moving Picture Experts Group
NFRP	Neurofibromatosis Research Program
NIH	National Institutes of Health
OMB	Office of Management and Budget
PDF	Portable Document Format
SOW	Statement of Work
TIFF	Tagged Image File Format
USAMRAA	US Army Medical Research Acquisition Activity
USAMRMC	US Army Medical Research and Materiel Command
USC	United States Code
WAV	Waveform