Investigator-Initiated Research Award

Decreasing the Impact of Neurofibromatosis (NF) and Schwannomatosis through Innovative Research

Basic science research constitutes the first steps toward understanding the fundamental questions of NF and Schwannomatosis.

The Investigator-Initiated Research Award supports basic or clinical studies by established researchers that will provide insight into the molecular mechanisms underlying the development of NF and lead to substantial improvements over today's approach to the diagnosis and treatment of NF1, NF2, and Schwannomatosis. Nested Postdoctoral Traineeships are also available under this award mechanism to prepare recent doctoral graduates for a career in NF research through a mentored training experience.

The program is especially interested in:

- Markers for disease progression or imaging methods
- Developmental and psychological aspects of disease
- Effects of hormones on disease progression
- Genetic and nongenetic factors that play a role in the determination of disease manifestations

Established research applicants must be independent investigators at the Assistant Professor level or higher. A maximum of $1.3 million in direct costs is available for up to 4 years, plus indirect costs as appropriate. Inclusion of preliminary data is required for all proposal submissions. Nested Postdoctoral Traineeships are available for investigators with 3 years or less experience as a postdoctoral fellow. Funding for Traineeships can be requested for a maximum of $55,200 per year in direct costs for up to 4 years, plus indirect costs as appropriate.

Proposals Are Due by:

March 14, 2006

This document is a synopsis of details specific to the Neurofibromatosis Research Program (NFRP) Investigator-Initiated Research Award. A detailed description of this award mechanism along with specific evaluation criteria, submission requirements, and deadlines are available in the FY05 NFRP Investigator-Initiated Research Award Program Announcement.

http://cdmrp.army.mil

Program Announcement

I. GENERAL INFORMATION

The Neurofibromatosis Research Program's (NFRP's) Investigator-Initiated Research Award supports basic or clinical studies by established researchers that will provide insight into the molecular mechanisms underlying the development of NF and lead to substantial improvements over today's approach to the diagnosis and treatment of NF1, NF2, and Schwannomatosis. Due to the success of this award mechanism in its initial presentation, the NFRP is currently offering a fast-track version of this award mechanism to be awarded no later than September 30, 2006. Please refer to Section III for funding award details.

A. Title of Award: NFRP Investigator-Initiated Research Award.

B. Program Name: Department of Defense (DOD) FY05 NFRP.

C. Funding Opportunity Number: W81XWH-05-NFRP-IIRA.

D. Agency Name: US Army Medical Research and Materiel Command (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 (W81XWH-05-NFRP-IIRA) 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 a.m. to 5 p.m. Eastern time at 301-682-5507. Help is also 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 implements its extramural research program predominantly through the award of grants and cooperative agreements. More information on these funding instruments may be obtained by request from:

Fax:	301-619-2937
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 downloading documents should contact the CDMRP as indicated in Subsection 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 Investigator-Initiated Research Award is part of the DOD NFRP, which was established in FY96 to promote research directed toward decreasing the impact of neurofibromatosis (NF). Appropriations for the NFRP since FY96 total $155.3 million (M). The program history of the FY96-04 NFRP is shown in Table 1. The FY05 NFRP appropriation is $25M. Of this, approximately $3.0M will be available for Investigator-Initiated Research Awards under this announcement. This program announcement is being released prior to the Congressional appropriation of FY06 funds. Should FY06 appropriations become available, these funds could be used to supplement the $3.0M currently available. However, a new FY06 Investigator-Initiated Research Award will not be offered.

Table 1. History of the DOD's Peer Reviewed NFRP

Program History	FY96-03	FY04
Congressional Appropriations for NFRP	$110.3M	$20M
Total Proposals Received	362	95
Total Proposals Funded	117	23[1]
Investigator-Initiated Research Award Proposals Received	168	18
Investigator-Initiated Research Award Proposals Funded	56	8

[1]Includes two FY03 proposals funded with FY04 appropriations

B. Program Objectives: The overall goal of the FY05 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 are 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 may be submitted from any eligible institutional source. Proposals are encouraged from investigators working at Historically Black Colleges and Universities/Minority Institutions (HBCU/MI).

C. Award Mechanism Description: The intent of the Investigator-Initiated Research Award is to sponsor basic and clinically oriented research that will (1) provide insight into the molecular mechanisms underlying the development of NF and related diseases; (2) result in substantial improvement(s) over today's approach to the diagnosis and treatment of NF1, NF2, and/or Schwannomatosis; and (3) enhance the quality of life for persons with those diseases. These grants are intended to fund independent investigators across a broad spectrum of disciplines. All Investigator-Initiated Research Award proposals must include preliminary data relevant to NF research and the proposed project. **In addition, if appropriate, the proposal should include a clear statistical plan of analysis.**

The FY05 NFRP encourages investigators to submit Investigator-Initiated Research Award proposals that:

- Define the genetic and nongenetic factors and modifiers that play a role in the manifestations of NF1, NF2, and/or Schwannomatosis, including tumor formation, growth, and progression in NF1 and NF2 tumors;
- Study the hormonal effects of puberty, pregnancy, and aging on disease progression and tumor growth;
- Develop new approaches for the quantification of the size, number, and/or growth rate of dermal neurofibromas;
- Address early childhood developmental and psychosocial aspects (e.g., learning disabilities and other cognitive aspects) of NF1;

- Develop new methods of imaging and measurement of lesions; and
- Develop surrogate markers for disease progression.

Investigator-Initiated Research Awards with Nested Postdoctoral Traineeship(s): Nested Postdoctoral Traineeships are being offered as an optional part of Investigator-Initiated Research Award proposals. The intent of the Nested Postdoctoral Traineeship is to enable doctoral degree graduates to either extend ongoing research related to NF or broaden the scope of their research to include work relevant to NF under the guidance of a designated mentor who is participating in the proposal. It is expected that the training will provide a valuable opportunity to further develop the experience necessary to advance the trainee's research career in NF.

A trainee is defined as a postdoctoral student with 3 years or less of postdoctoral experience at the time of proposal submission. Eligible postdoctoral candidates must have successfully defended a doctoral thesis and completed all academic requirements at the time of award negotiations.

There is no limit to the number of postdoctoral trainees that can be nested within a given Investigator-Initiated Research Award proposal. However, these Nested Postdoctoral Traineeships can only be obtained as an optional part of the Investigator-Initiated Research Award mechanism. Applicants must submit a biographical sketch of no more than four pages for each trainee and include it in the biographical sketch section. "To be named" trainees are acceptable for the proposal submission. For proposals approved for funding, the US Army Medical Research Acquisition Activity (USAMRAA) requires the name and biographical sketch of each applicant for review and approval.

III. AWARD INFORMATION

Funding for Investigator-Initiated Research Awards may be requested for a maximum of $1.3M in direct costs over a 4-year performance period, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, and travel to scientific/technical meetings. The amount for this travel may not exceed $1,800 per year. Institutional support and commitment must be evident to foster the applicant's research career, such as the provision of access to adequate laboratory facilities and equipment. Although not required, multi-institutional and multidisciplinary research collaborations are encouraged.

Funding for Nested Postdoctoral Traineeships may be requested as part of the $1.3M total. There is no limit to the number of postdoctoral trainees that may be nested within a given Investigator-Initiated Research Award proposal. Funding for each traineeship can be requested for a maximum of $55,200 per year in direct costs for a maximum of $220,800 per trainee for up to 4 years, plus indirect costs as appropriate. Direct costs can cover salary; stipends; seminars and courses; and expenses including research supplies, equipment, and travel to scientific meetings. Expenses relevant to the traineeship should be listed under the "Other" category on the Detailed Cost Estimate form.

The nature of this Program does not allow for renewal of grants or supplementation of existing grants. Approximately $3.0M is available for this award mechanism. Depending on the number and quality of the applications, it is anticipated that approximately one or two proposals will be funded. This program announcement is being released prior to the Congressional appropriation of FY06 funds. Should FY06 appropriations become available, these funds could be used to supplement the $3.0M currently available. In this scenario, additional proposals submitted to this FY05 mechanism may be funded. However, a new FY06 Investigator-Initiated Research Award will not be offered.

IV. ELIGIBILITY INFORMATION

A. Applicants: Applicants must be independent investigators at the Assistant Professor level (or equivalent) or higher.

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." To protect the public interest, the Federal Government ensures the integrity of Federal programs by conducting business with responsible recipients only. 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's 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 if 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, 2006, 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, that will be used to carry over funds between fiscal years.

[1]Executive Orders 12876, 12900, and 13021

C. Duplicate Submissions: Submission of the same research project to the NFRP under different 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.

The applicant is responsible for entering and/or uploading the following information into the CDMRP eReceipt system at https://cdmrp.org:

- **Letter of Intent (LOI):** Enter a brief description of the proposal or the LOI in a data field under "My Proposals: Create New Proposal." The LOI is generated when the "Save and Forward Letter of Intent" option is chosen.
- **Proposal Information:** Enter the Proposal Information in data fields under the "Proposal Information" tab.
- **Proposal Contacts:** Contact information for both the applicant and the Contract Representative is required under the "Proposal Contacts" tab.
- **Collaborators and Conflicts of Interest (COI):** Information about collaborators and other individuals outside the scope of the proposal, who may have a COI in the review of this proposal, is captured in data fields under the "Collaborator/COI" tab.
- **Proposal Abstracts, Impact Statement, and Statement of Work (SOW):** The Technical Abstract, Public Abstract, Impact Statement, and SOW are each entered in a separate data field under the "Abstract/Impact/SOW" tab.
- **Proposal Main Body:** Uploaded as a PDF file under the "Required Files" tab.
- **Supporting Documentation:** Uploaded as a PDF file under the "Required Files" tab.
- **Budget Information:** Uploaded as a PDF file under the "Required Files" tab.
- **Regulatory Documents:** The Certificate of Environmental Compliance and the Principal Investigator Safety Program Assurance form are uploaded as separate PDF files under the "Required Files" tab.

The Contract Representative or equivalent responsible for sponsored program administration at the applicant's institution is responsible for the following:

- **The Contract Representative's Contact Information Profile:** This must be completed before electronic approval of all submission components.
- **US Army Medical Research Acquisition Activity (USAMRAA)-Required Documents:** The institution's currently negotiated "Rate Agreement," "Certifications and Assurances for Assistance Agreements," and the "Representations for Assistance

Agreements" are uploaded as separate PDF files under the Contract Representative's "My Profile" tab.

- **Approval:** The Contract Representative must approve all submission tabs (Proposal Information, Proposal Contacts, Collaborators and COI, Abstracts/Impact Statement/SOW, Required Files). Contract Representative approval must occur before the submission deadline of 5:00 p.m. Eastern time, March 14, 2006. The eReceipt system will ***not*** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time deadline.

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 appropriate software and learn the process before 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 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 inches (approximately 19 cm x 25.5 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. Insertion 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. ***Nonadherence 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 prior to peer review:

- Proposal body exceeds page limit.
- Proposal body is missing.
- Detailed cost estimate is missing.
- Proposal is incomplete after the deadline.

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

Any 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 prior to electronic submission, it is strongly recommended that applicants review their files to ensure that the proposal complies with the preparation guidelines outlined in this program announcement.

D. Letter of Intent (LOI): A Letter of Intent should be submitted by **February 14, 2006** at https://cdmrp.org. A brief description of the proposal is entered in a data field under "My Proposals: Create New Proposal." The LOI is generated when the "Save and Forward Letter of Intent" option is chosen. The LOI may be modified under "Proposal Information" at any time until the applicant submits this information by choosing the "Finalize for CR Approval" option.

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 will be generated from the information uploaded in the CDMRP eReceipt system and electronically appended to the proposal by the CDMRP eReceipt system.

F. Proposal Contacts: The Proposal Contacts ***must*** include the e-mail address of a Contract Representative in the Sponsored Programs Office (or equivalent) authorized to negotiate on behalf of the applicant's institution. The Proposal Contacts must be approved by the Sponsored Programs Office (or equivalent) representative at the applicant's institution.

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

H. Proposal Abstracts – 5,700-character limit, including spaces (approximately one page), for each abstract: Each abstract should include the name of the PI and the title of the proposal. A structured technical abstract and a public (nontechnical) abstract are required. These abstracts are vitally important to both the peer and programmatic review process. 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 paramount that the Principal Investigator (PI) describe the proposed work fully in the abstracts to be submitted. Each abstract must be entered into the appropriate data field under the "Abstract/Impact/SOW" tab of the CDMRP eReceipt system.

Applicants may key 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 https://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 https://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:** Provide a brief statement of 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 concisely the specific aims of the study.
- **Study Design:** Briefly describe the study design.
- **Relevance:** Provide a brief statement explaining the relevance of the proposed work to the Program's goals. For example, describe how the study will cure, prevent, or improve the detection or treatment of the disease.

2. Public Abstract: Sample public abstracts can be found at https://cdmrp.org/samples.cfm. The public abstract is intended to communicate the purpose of, and rationale for, the study to nonscientific audiences. The public abstract is an important component of the proposal review process because consumer advocates, who play an integral role in the review and funding decision process, use this abstract as they review the proposal. The public abstract must be written such that the scientific objectives and rationale for the proposal can be readily understood by non-scientists. ***The public abstract must not***

duplicate the technical abstract. It should describe the goals and objectives of the research project, its relevance to the Program, and/or its potential impact on the disease or the field.

In addition to describing the project, the public abstract must answer the following questions:

- What will the ultimate applicability of the research be?
  - What types of patients will it help, and how?
  - 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, what are 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 in a data field under the "Abstract/Impact/SOW" tabs in the CDMRP eReceipt system. Applicants may key the Impact Statement or "cut and paste" it from a word processing application into the data field.

The PI must state explicitly how the proposed work will make an original and important contribution to the NF and/or Schwannomatosis research fields**.** Describe clearly the impact of this study on the concepts and methods that drive the field(s) and or the impact on the diagnosis or 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 review, is often cited by consumer advocates during the review and funding processes.***

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

The SOW is a concise restatement of the research proposal, outlining, step by step, how each of the major goals or objectives of the proposed research/services will be accomplished during the period for which the USAMRMC will provide financial support. When a proposal is submitted requesting funding for part of a larger study, the proposal's SOW must include DOD-funded tasks only. Sample SOWs can be found at https://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 period of the proposed effort;

- Allow four to six months for regulatory review and approval processes for human use studies;
- Allow two 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. The page limit for the Project Description is **20 pages** inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other relevant information needed to judge the proposal. **Applicants requesting funding for Nested Postdoctoral Traineeships must also submit a Nested Postdoctoral Traineeship Proposal Body (see below) as part of the proposal main body. Applicants may include up to 4 additional pages per trainee in the proposal main body for the Nested Postdoctoral Traineeship Proposal Body.**

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

Upload the proposal main body (including the Nested Postdoctoral Traineeship proposal body, as appropriate) as a PDF file under the "Required Files" tab.

The inclusion of preliminary data ***is required*** for all Investigator-Initiated Research Award proposal submissions. Investigators must submit promising and well-founded preliminary data relevant to NF and the proposed project.

1. Project Description. Describe the proposed project using the outline provided below; 20-page limit inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other relevant information needed to judge the proposal.

- **Background:** Describe the ideas and reasoning behind the proposed work and previous experience most pertinent to the proposal. Cite relevant literature references.
- **Rationale:** State the purpose of the study and the expected results.
- **Objectives:** State concisely the specific aims of the study. When submitting a proposal requesting funding for part of a larger study, the aims and research strategy should be presented only for DOD-funded tasks. The applicant must address how the research plan will be affected if all large study components do not receive funding, e.g., Can the DOD-funded research be completed as proposed if funding is not received for all components? What adjustments would be needed in the study design to meet such a contingency?

- **Preliminary Data:** Provide pertinent data to support the necessity, feasibility, and potentiality of the proposed project.
- **Methodology:** Describe the experimental design and methodology, including statistical analysis. If using either human subjects or human biological samples, include a plan for the recruitment of subjects and/or the acquisition of samples.

2. Nested Postdoctoral Traineeship Proposal Body (required for applicants requesting funding for Nested Postdoctoral Traineeships): Start section on a new page; four-page limit per trainee. Describe the following for each trainee: Identify the staff members who are responsible for the trainee. Describe the research training plan including a timeline, laboratory techniques, conferences, seminars, journal clubs, teaching responsibilities, and/or clinical responsibilities. Describe how the research being performed under the PI's direction is relevant to NF and/or Schwannomatosis. Describe the PI's history of training other Postdoctoral students. Specify how the PI will assist in training the Postdoctoral student for a career in NF and/or Schwannomatosis research. Describe the laboratory's resources to demonstrate the adequacy of support for the trainee's project.

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 relevant 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 requiring signatures must be signed and incorporated into the supporting documentation file prior to its submission.

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 any postdoctoral trainees, clinical coordinators, 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 Biographical Sketch form may be used. Use of this form is not mandatory, but the information requested should 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 PI and key personnel on a separate page. If no support exists, state "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 are included in the submission, the extra items will not be peer reviewed.

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

1. Funding Restrictions: Funding for Investigator-Initiated Research Awards can be requested for a maximum of $1.3M in direct costs over a 4-year performance period, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, and travel to scientific/technical meetings. The amount allotted for this travel is $1,800 per year.

Funding for Nested Postdoctoral Traineeships can be requested as part of the $1.3M total. There is no limit to the number of postdoctoral trainees that can be nested within a given Investigator-Initiated Research Award proposal. Funding for each traineeship can be requested for a maximum of $55,200 per year in direct costs, for a maximum of $220,800 per trainee for up to a 4-year performance period, plus indirect costs as appropriate. Direct costs can cover salary, stipends, seminars and courses, expenses including research supplies, equipment, and travel to scientific meetings. Expenses relevant to the traineeship should be listed under the "Other" category on the Detailed Cost Estimate form.

2. Detailed Cost Estimate Form and Budget Justification Instructions: Budget is an important consideration in both peer and programmatic review, and applicants are cautioned

to use discretion in budget requests. Budgets also will be reviewed during award negotiations. ***Applicants 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 US 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. ***Institutions are expected to 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 PI, 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 (PI) 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 PI'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. Because the coordination of clinical research and/or clinical trials is a time-consuming and complex process, any clinical trial must have a clinical coordinator who has sufficient time dedicated to the project to carry out the record-keeping, coordination, and/or other administrative duties the project entails.

vi. Salaries Requested: Enter the salaries in whole dollar figures for each position for which funds are requested. The salary requested is calculated by multiplying an individual's institutional base salary by the percentage of effort on the project.

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

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 separately negotiated.

i. If the purchase of equipment for this research project is requested, it is expected that institutions 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 total estimated 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 are to 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. Funding for travel outside the United States requires prior approval from USAMRAA.

f. Research-Related Subject Costs: Itemize costs of subject participation in the research study. These costs are strictly limited to expenses specifically associated with the proposed study. The USAMRMC will not provide funds for ongoing medical care costs 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 under 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 US 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, 2006, 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, that will be used to carry over funds between fiscal years.

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 prior to the submission deadline of **5:00 p.m. Eastern time, March 14, 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 (Research Involving Human Subjects and/or Anatomical Substances/Cadavers; Research Involving Animals) with the proposal. The applicant should provide these documents to the USAMRMC only upon request.

O. USAMRAA-Required Documents: The most current version of the institution's negotiated "Rate Agreement," the "Certifications and Assurances for Assistance Agreements," and the "Representations for Assistance Agreements" must be uploaded by the Contract Representative at the applicant's institution. 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 in the Sponsored Programs Office (or equivalent) 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, March 14, 2006, deadline.

The timeline for the Investigator-Initiated Research Award is:

Online Letter of Intent:	Expected by **February 14, 2006**
Online Proposal Information:	Prior to proposal submission
Proposal Submission/Approval Deadline:	**5:00 p.m. Eastern time, March 14, 2006**
Peer Review (First Tier):	May 2006
Programmatic Review (Second Tier):	June 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:	September 2006

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

Several steps are critical to successful proposal submission:

- The Proposal Information must be "saved as final" before the proposal is submitted. Applicants are encouraged to begin this part of the submission process early.
- Proposal Contacts must be "saved as final" before the proposal is submitted. The e-mail address of a Contract Representative in the Sponsored Programs Office (or equivalent) 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 Sponsored Programs Office (or equivalent) early in the application process.
- The Contract Representative in the Sponsored Programs Office (or equivalent) 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, March 14, 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 peer review 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: Investigator-Initiated Research Award proposals will be evaluated according to the following criteria:

- **Research Strategy:** Are the conceptual framework, hypotheses, design, methods, and analyses adequately developed and well integrated to the aims of the project? Is a clear-cut rationale supporting the research provided? Does the applicant acknowledge potential problem areas and consider alternative methods/tactics? Do the required preliminary data in NF and/or Schwannomatosis research support the proposed project? Is the experimental design sound and sufficiently well-developed with the required statistical power to lead to significant results?
- **Significance and Impact:** To what extent will the project make an original and important contribution to the field of NF and/or Schwannomatosis research? What will be the impact of this study on the concepts or methods that drive the field? What will be the impact of the project on the treatment of NF and/or Schwannomatosis? What are the potential clinical applications, benefits, and risks?
- **Principal Investigator and Personnel:** Is the PI appropriately trained and well-suited to carry out this work? Does the PI show potential for contribution to the NF and/or Schwannomatosis fields? Does the PI have the appropriate knowledge, skills, and abilities to complete the proposed project? Is appropriate expertise available to conduct the study successfully? **For Investigator-Initiated Research Awards with Nested Postdoctoral Traineeship(s)**: Do the PI and other scientific personnel have the background, qualifications, research resources, and time to supervise the Postdoctoral trainee? Is there a senior staff member who is identified and responsible for the trainee(s)? What is the mentor's previous research training experience with Postdoctoral trainees? Does the mentor have experience in NF and /or Schwannomatosis research?
- **Environment:** Is there evidence that the scientific environment is an appropriate setting for the proposed research? Is there evidence that the research requirements are adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed? Is there evidence of institutional support provided with the proposal? **For Investigator-Initiated Research Awards with Nested Postdoctoral Traineeship(s):** Is the research training properly structured and balanced to ensure that the trainee(s) will acquire the knowledge and necessary skills relevant to the area of NF and/or Schwannomatosis being studied? Is the proposed research likely to provide the trainee with a strong foundation in NF and/or

Schwannomatosis research that will prepare and encourage him or her to follow a career path in this area? Will the training take place in an environment that is appropriate for the trainee to accomplish his or her goals? Is evidence provided that the research and training requirements are adequately supported by the resources and proposed collaborative arrangements?

- **Budget:** Is the budget appropriate for the research proposed? Is there evidence that, where appropriate, arrangements have been made to compensate human subjects/participants for expenses they incur from participating in the project?

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

- Ratings and evaluations of the scientific and consumer peer reviewers,
- Programmatic relevance,
- Relative innovation,
- 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. Applicants can expect to receive this notification approximately 4 weeks after programmatic review. A copy of the peer review summary statement will be posted to the CDMRP eReceipt system.

B. Administrative Requirements: Awards are made to organizations, not individuals. A PI must submit a proposal through, and be employed by or affiliated with, a university, college, nonprofit research institution, commercial firm, or Government agency (including military laboratories) to receive support. A prospective recipient must meet certain minimum standards pertaining to institutional support, financial resources, prior 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 home page at http://www.ccr.gov.*

Proposals from Federal agencies ***must*** provide a plan delineating how all funds will be obligated by September 30, 2006, 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, that will be used to carry over funds between fiscal years.

A change in institutional affiliation will require that the PI resubmit the entire proposal packet through the new Institution to include any regulatory documentation that may require protocols, etc., to be re-approved for the new Institution. The original institution must agree to relinquish the award. Any delay in the submission of the new information will result in a delay in contracting and regulatory review and a subsequent delay in resumption of work on the project. **Transferring an award that includes a Phase I, Phase II or a 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 in the Sponsored Programs Office (or equivalent) 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.

Collaborating institutions participating in multi-institutional studies must be committed to resolving all potential intellectual and material property issues and to removing all institutional barriers that could impede full cooperation. 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, 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 also required; it will be requested at a later date. A Facility Safety Plan from the applicant's institution may have been previously received 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 this 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 work involving animals. PIs must complete and submit the animal use appendix titled "Research Involving Animals," which can be found on the ACURO website, https://mrmc-www.army.mil/rodorpaurd.asp).

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: (See Subsection V.N for information pertaining to the submission of documents related to the use of human subjects, human biological substances, and/or 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 is also 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 that this instruction has been completed will be required during the regulatory review process.

Timely resolution of human subjects protocols submitted to the investigator's local IRB is expected.

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 980 that are applicable to DOD-sponsored research before writing a research protocol. Title 10 United States Code 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; 42 USC 289g through 289g-2[2]; US Food and Drug Administration regulations; and any other applicable Federal, state, and local laws and regulations.

[2]Title 42 United States Code, Sections 289g through 289-2

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

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

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

e. Clinical Trial Registry: All PIs are required to register clinical trials individually on www.clinicaltrials.gov using a Secondary Protocol ID number designation, "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") are required register, to include all Phase I-IV clinical trials, as well as trials that do not fit into one or more phases, but that are clearly interventional or observational (e.g., some epidemiological or behavioral studies). Questions on registration should be addressed to the 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 applied-for written approvals directly to the applicant.

E. Reporting Requirements: Reports are required for continuation of the research and funding. Each award instrument will state the reports that are due to the Government. (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 report.

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

3. Non-Exempt Human Studies Reports: For non-exempt human subjects research, documentation of local 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: PIs 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 visual interleave
CCR	Central Contractor Registration
CDMRP	Congressionally Directed Medical Research Programs
CFDA	Catalog of Federal Domestic Assistance
COI	Conflict of Interest
CR	Contract Representative
DOD	Department of Defense
EPLS	Excluded Parties List System
FAR	Federal Acquisition Regulations
FY	Fiscal Year
HBCU/MI	Historically Black Colleges and Universities/Minority Institutions
HSRRB	Human Subjects Research Review Board
IIRA	Investigator-Initiated Research Award
IRB	Institutional Review Board
JPEG	Joint Photographic Experts Group
LOI	Letter of Intent
M	Million
MPEG	Moving Picture Experts Group
NF1	Neurofibromatosis Type 1
NF2	Neurofibromatosis Type 2
NFRP	Neurofibromatosis Research Program
NIH	National Institutes of Health
OMB	Office of Management and Budget
PDF	Portable Document Format
PI	Principal Investigator
TIFF	Tag Image File Format
URL	Uniform Resource Locator
USAMRAA	US Army Medical Research Acquisition Activity
USAMRMC	US Army Medical Research and Materiel Command
USC	United States Code
WAV	Wave