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FOREWORD

The U.S. Army Medical Research and Materiel Command (USAMRMC) has been directed by the Secretary of the Army to continue the Department of Defense (DOD) Neurofibromatosis Research Program (NFRP). The deadline, format, and other criteria specified for proposals in this NFRP Announcement are based on program objectives, public needs, and regulatory guidance.

General information on the USAMRMC can be obtained from the USAMRMC website (*http://mrmc-www.army.mil*). Specific information on the DOD NFRP can be obtained from the USAMRMC Congressionally Directed Medical Research Programs (CDMRP) website (*http://cdmrp.army.mil*). A copy of this Announcement and associated forms (except for the Proposal Cover Booklet; see Section 3 below) can also be downloaded from the USAMRMC CDMRP website (*http://cdmrp.army.mil*).

1. Inquiries

Questions concerning the preparation of proposals, formats, or required documentation can be addressed to the USAMRMC at:

Fax: (301) 619-7792
Phone: (301) 619-7079
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP99-Announcement)
524 Palacky Street
Fort Detrick, MD 21702-5024

Every effort will be made to answer questions within 10 working days of receipt. Inquiries should be restricted to format issues only; no questions relating to technical proposal content or reasonableness/allowability of costs will be answered. Applicants should submit any written questions regarding this program as early as possible.

2. Forms

Associated forms (except for the Proposal Cover Booklet; see Section 3 below) can be found in the Appendices of the NFRP Fiscal Year 1999 Program Announcement. The June 4, 1999 Program Announcement can be downloaded from the USAMRMC CDMRP website (*http://cdmrp.army.mil*).

3. Proposal Cover Booklet (Bubble Sheet)

A Proposal Cover Booklet must be completed for each submission according to the instructions found in Appendix B.

Proposal Cover Booklets must be requested via fax, phone, e-mail, or mail at the following addresses/numbers. Please allow sufficient time for delivery by regular mail.

Fax: (301) 682-5521
Phone: (301) 682-5501
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP99-Program Announcement)
524 Palacky Street
Fort Detrick, MD 21702-5024

4. Proposal Submission

To be considered for award, submit the following documentation to the address at the end of this subsection:

Proposal: **ONE** clearly labeled original (binder-clipped) and **THIRTY** collated photocopies (stapled or binder-clipped) of the **entire package**. **Every copy must match the original.** Do not use rubber bands, or spiral or three-ring binders.

Proposal Cover Booklet: **ONE** original (binder clipped to the original proposal) and **THREE** photocopies (***not*** binder-clipped to proposal copies).

Letters of Recommendation: If required, binder-clipped to the front of original proposal under the original Proposal Cover Booklet. See individual application instructions.

Abstract Pages: An additional **FIVE** copies of both the technical and the public (non-technical) abstracts in a manila envelope along with a 3½" computer disk containing the abstract pages [clearly labeled with the name of the principal investigator (PI), institution, and word processing program]. It is recommended that abstracts be formatted in Word, WordPerfect, or ASCII. **Note:** The abstracts are ***vital*** to the review of the proposal. Abstracts of all funded proposals will be reproduced in an NFRP abstract book and posted on the CDMRP website *(http://cdmrp.army.mil)*.

Packaging: Package only **ONE** complete proposal submission (original plus all copies requested above) per box. If acknowledgment of proposal receipt is desired, enclose a self-addressed, stamped postcard with each submission. This postcard should state the proposal title and PI's name.

Send the Proposal to:
Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP99-Announcement)
1076 Patchel Street (Building 1076)
Fort Detrick, MD 21702

5. Deadline

The deadline for receipt of ***all submissions*** is **September 15, 1999 at 4:00 p.m. Eastern Time**.

Any proposal received by the USAMRMC after the exact time specified for receipt shall ***not*** be considered unless it is received before award is made, and it:

1. was sent by mail, and it is determined by the Government that late receipt was due solely to mishandling by the Government after receipt at the Government installation, or

2. was sent by U.S. Postal Service Express Mail Next Day Delivery (Post Office to Addressee: ***Do not use Second Day Delivery***) and postmarked no later than 8:00 p.m. (local time at point of origination) the day before the proposal receipt deadline, or

3. was placed into the control of a commercial courier service no later than 8:00 p.m. (local time at point of origination) the day before the proposal receipt deadline for delivery by 4:00 p.m. Eastern Time on the due date.

Investigators are advised that documentation of time of receipt by the delivery agent may be necessary if a problem should occur.

6. Timeline

Proposal Receipt:	September 15, 1999
Peer Review:	November 1999
Request for Appendices:	Approximately 2 weeks after the completion of peer review
Programmatic Review:	January 2000
Notification:	February 2000
Award Date:	No later than September 30, 2000

Driving Directions to Fort Detrick

Directions from Washington, DC

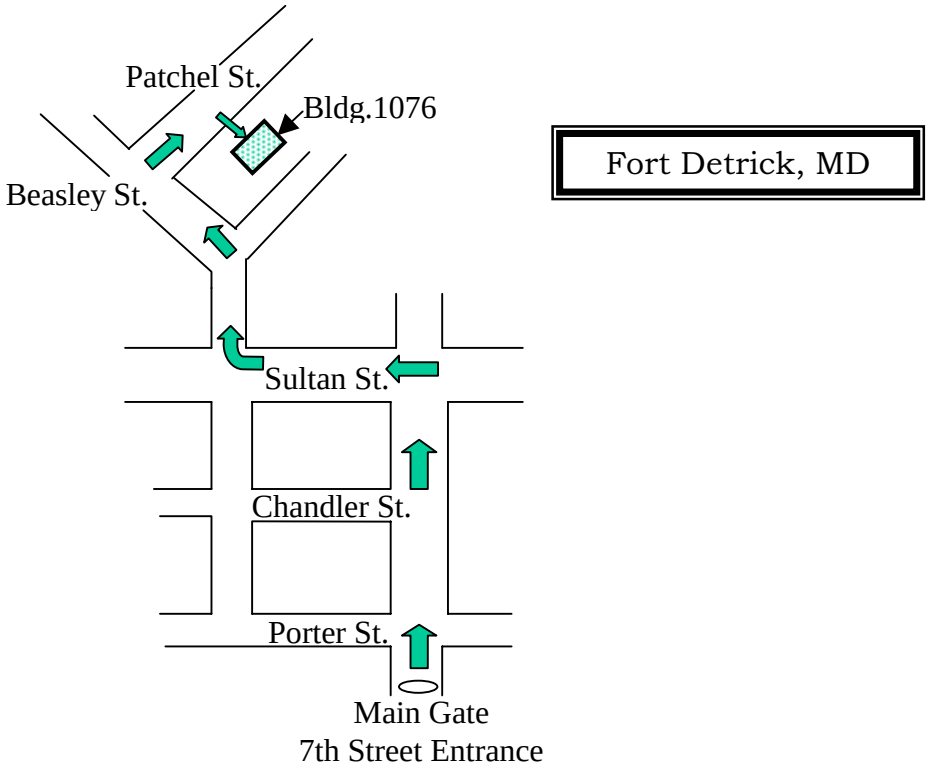
Take Interstate 495 to Interstate 270 North (exit #38) toward Rockville, Maryland. At Frederick, Interstate 270 ends and joins Route 15 North. Follow Route 15 North to 7th Street exit. Turn right on 7th Street and go four blocks to Fort Detrick's Main Gate.

Directions from Baltimore, MD

Take Interstate 695 to Interstate 70 West. In Frederick, take exit 53, Route 15 North. Follow Route 15 North to 7th Street exit. Turn right on 7th Street and go four blocks to Fort Detrick's Main Gate.

Map of Fort Detrick

Packages to be delivered to the Neurofibromatosis Research Program should be delivered to building 1076 as shown on the map below. To gain entry to Ft. Detrick, you will be required to show your driver's license at the Main Gate. Please allow at least 15 minutes to pass through gate area.



Reference Table of Award Mechanisms and Submission Requirements

Award Mechanisms	Experience of PI	Key Category Elements	Dollars Available	Proposal Submission Deadline	Instructions for Proposal Preparation
Idea Awards	All levels of experience	• Reward innovative ideas and technology • No preliminary data required	An average of $100,000 per year in direct costs, for a maximum of $200,000 over 2 years, plus indirect costs as appropriate	September 15, 1999 4:00 p.m. ET	Section III
New Investigator Awards	An independent investigator: (a) Assistant Professor or equivalent with no more than 6 years of experience in the field of NF, ***or*** (b) a more senior investigator new to the field	• To support research on an issue relevant to NF • No preliminary data required	An average of $100,000 per year in direct costs, for a maximum of $300,000 over 3 years, plus indirect costs as appropriate	September 15, 1999 4:00 p.m. ET	Section IV
Investigator-Initiated Research Awards (with or without Nested Post-doctoral Traineeship)	An independent investigator (at least an Assistant Professor or equivalent)	• To sponsor basic research leading to clinical trials relevant to NF • To fund investigators across a broad spectrum of disciplines • Preliminary data required	• There are no total dollar amount restrictions to these awards • Funding can be requested for up to 3 years only • With Nested Post-doctoral Traineeship: a maximum of $48,000 per year inclusive of direct and indirect costs for a maximum of $144,000 per trainee over 3 years • There is no limit on the number of post-doctoral trainees nested under a given proposal	September 15, 1999 4:00 p.m. ET	Section V
Clinical Trial Awards	Investigators with clinical trial experience	• To sponsor Phase 1 or Phase 2 clinical trials of any novel therapeutic approach for NF1 or NF2 • ***IRB approval and informed consent form from at least one participating institution must be submitted with the proposal by the receipt deadline*** • Preliminary data required	• There are no total dollar amount restrictions to these awards • Funding can be requested for up to 3 years only	September 15, 1999 4:00 p.m. ET	Section VI

I. Overview of the Congressionally Directed Medical Research Programs

I-A. History of the Congressionally Directed Medical Research Programs

In the past decade, the work of consumer advocacy organizations has dramatically influenced the way scientific research is funded in this country. Beginning in fiscal year 1992 (FY92), the U.S. Congress has directed the Department of Defense (DOD) to manage various extramural and intramural grant programs targeted toward specific research initiatives. The U.S. Army Medical Research and Materiel Command (USAMRMC) constituted the office of the Congressionally Directed Medical Research Programs (CDMRP) to administer these funds. To date, $1.1 billion has been targeted by Congress for research on breast cancer, prostate cancer, ovarian cancer, neurofibromatosis (NF), Defense women's health, and osteoporosis. Together, these six programs are managed by the CDMRP.

For each appropriation, the CDMRP has developed and refined a flexible 6-year execution and management cycle that spans the development of an investment strategy through the completion of research. A Program Staff, composed of military and civilian scientists and clinicians, manages the CDMRP programs. For each program, an expert Integration Panel (IP) of scientists, clinicians, and consumer advocates is convened to deliberate issues and concerns unique to their program, to establish an appropriate investment strategy, and to perform programmatic review as described in Section I-B.2. Based upon this investment strategy, each program then employs a variety of award mechanisms to address the most urgent needs of a research community.

Overall, the CDMRP exists to support research that will impact upon the health of all Americans. The CDMRP strives to identify gaps in funding and provide award opportunities that will enhance program research objectives without duplicating existing funding opportunities. In meeting their goals, the CDMRP has developed unique mechanisms to facilitate funding of quality research that addresses individual program objectives.

I-B. Proposal Evaluation

The CDMRP uses a two-tiered review system for proposal evaluation, which consists of scientific merit review and programmatic review, as recommended by the National Academy of Science's Institute of Medicine. The two tiers are fundamentally different. The first tier is a peer review of proposals against established criteria for determination of scientific merit. The second tier is a programmatic review of proposals that compares submissions to each other and recommends proposals for funding based on program goals.

I-B.1. Scientific Peer Review

Scientific peer review is conducted by panels organized by scientific discipline or specialty area. The primary responsibility of the scientific peer review panels is to provide unbiased, expert advice on the scientific and technical merit of applications, based upon the review criteria developed for each award mechanism.

Each scientific review panel is composed of a chair, scientific reviewers, consumer reviewers, and a non-voting executive secretary. The chair and scientific reviewers are recognized leaders in their fields and are chosen on the basis of their scientific expertise. Selection of individuals as scientific reviewers is predicated upon their expertise as well as their experience in scientific peer review. For the purposes of the NFRP, consumers are defined as individuals with NF, their family members, or representatives of consumer organizations. Consumer reviewers augment scientific merit review by bringing the patient and family perspectives to the assessment of science and relevance of the research.

Panel members rate each proposal based on the specific evaluation criteria developed for each award category (see Sections III-B, IV-B, V-B, and VI-B). Two types of ratings are used. First, each of the evaluation criteria, except for the budget, is rated on a scale of 1 (low merit) to 10 (high merit). This criteria scoring ensures that each component is considered in peer review. Second, the overall proposal is given a global score using a scale of 1 (high merit) to 5 (low merit). Criteria scores are neither averaged nor mathematically manipulated to determine the global score. Instead, reviewers are asked to use the criteria scores as a guide in determining the global score. A proposal may be disapproved at scientific peer review if it is so seriously flawed as to make its completion implausible, or if gravely hazardous or unethical procedures are involved.

The proposal summary statement is a product of scientific peer review. Each statement includes the investigator's technical and public (non-technical) abstracts (verbatim), the peer review global score, and an evaluation of the project as assessed by the peer reviewers according to evaluation criteria published in this Announcement. Summary statements not only assist investigators in assessing their research projects, but are forwarded to the next stage of the review process, programmatic review.

I-B.2. Programmatic Review

The second tier of the two-tiered review system is a programmatic review of the proposals considered eligible for funding. Programmatic review is accomplished by an IP composed of scientists and consumer advocates. The scientific members of the IP represent many diverse disciplines and specialty areas, and are experienced with peer review procedures. Consumer advocates represent national advocacy constituencies and are full voting members of the IP. With their firsthand experience, the consumer advocates enhance the review process by focusing attention upon critical patient issues and outcomes. The function of the IP is to conduct

programmatic review to obtain a broad portfolio of grants across all disciplines and recommend an investment strategy for appropriated funds.

Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool. IP members use the peer review summary statements to review proposals. The Statement of Work may also be reviewed at this level. However, the full proposal is not forwarded for programmatic review.

Programmatic review balances the potential outcomes and risks of scientifically excellent proposals. It should be emphasized that the IP is committed to funding a broad-based research portfolio. While the ratings and recommendations of peer review panels are important factors in programmatic review, the IP must also consider other criteria to establish this portfolio. The criteria the IP uses to make funding recommendations are:

- ratings and recommendations of the peer review panels;
- programmatic relevance;
- scientific innovation; and
- program portfolio balance with respect to research disciplines or specialty areas.

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program are most likely to be recommended to the Commanding General, USAMRMC, for funding.

II. Department of Defense Neurofibromatosis Research Program

II-A. History of the Neurofibromatosis Research Program

Grassroots advocacy movements have heightened public awareness of NF as a significant health issue. In FY96, federal budgetary opportunities spurred Congress to appropriate increased funds to the DOD budget for the creation of an NF research program. The DOD used the model established through recommendations from the Institute of Medicine for USAMRMC Breast Cancer Research Program (BCRP) to establish the Neurofibromatosis Research Program (NFRP). Like the BCRP, the NFRP implements a two-tiered scientific review process that funds meritorious research that fulfills Program goals. The Program's success has encouraged Congress to appropriate additional funds to the NFRP in subsequent years, culminating in an $11.5M appropriation for the FY99 NFRP. Table II-1 provides an overview of the funding levels and awards made for FY96 through FY98 NFRP.

Table II-1: Program History

Fiscal Years	**1996**	**1997**	**1998**[**]
NFRP Congressional Appropriations	$8M	$8M	$9.8M
Number of Research Proposals Received	63	2	21
Number of Research Awards	13[*]	2	10
Percentage of Applications Recommended for Funding	21%[*]	100%	48%

[*] Three FY96 Investigator-Initiated Research Award proposals on the alternate funding list were funded with FY97 monies.

[**] Final numbers for FY98 will be available after September 30, 1999.

II-B. FY99 Program Emphasis Areas

The USAMRMC, through this NFRP Announcement, is soliciting applications for the following four award mechanisms: (1) Idea Awards; (2) New Investigator Awards (NIAs); (3) Investigator-Initiated Research Awards (IIRAs); and (4) Clinical Trial Awards (CTAs). The USAMRMC is challenging the scientific community to design innovative research that will foster new directions for, address neglected issues in, and bring new investigators into the field of NF research. As in previous years, the central theme of the NFRP continues to be research with a strong potential to lead to effective treatment of NF.

Prospective responders familiar with USAMRMC programs from previous years are urged to review this Program Announcement carefully, as revisions to award category definitions and submission requirements have been made.

Approximately $9.3M will be allocated for Idea Awards (Section III), NIAs (Section IV), IIRAs (Section V), and CTAs (Section VI). The intent of Idea Awards is to stimulate and reward creative research ideas that may be viewed as speculative but have the potential for high payoff. The intent of NIAs is to prepare new, independent scientists for careers in NF research and to present an opportunity to attract established investigators new to the NF field. In turn, the intent of IIRAs is to sponsor basic research relevant to NF. Finally, the USAMRMC is currently soliciting the submission of Phase 1 or Phase 2 CTA proposals for NF1 or NF2.

II-C. Participation of Juvenile Subjects

For proposals intending to recruit juvenile subjects, special attention must be paid to voluntary participation of juvenile subjects as described in Appendix H, part 5-b.iv.

III. Idea Awards

III-A. Idea Awards

The intent of Idea Awards is to encourage innovative approaches to NF research. These proposals may represent a new paradigm in the study of NF, challenge existing paradigms, or look at an existing problem from a new perspective. The proposed studies may be untested, but with a high probability of revealing new avenues of investigation. Although this research is inherently risky in nature, the research plan must demonstrate solid scientific judgment and rationale. The USAMRMC's Office of the CDMRP is currently soliciting the submission of Idea Award proposals from investigators of all levels of experience and from a broad spectrum of disciplines.

Idea Award proposals are qualitatively different from traditional research proposals as outlined in Table III-1 below. The inclusion of preliminary data is not required for Idea Award proposals; however, investigators must demonstrate a sound scientific rationale established through a critical review and analysis of the literature and/or logical reasoning. It is the responsibility of the investigator to clearly articulate how the proposed research is innovative. A letter of institutional support and commitment, demonstrating availability of laboratory facilities, equipment, and intent to foster the applicant's research career is required (see Section III-E, item 15).

Table III-1: Differences between Traditional Research Proposals, Idea Research Proposals, and New Investigator Award Proposals

Type of Proposal	Preliminary or Pilot Data	Description of Award Mechanism
Traditional Research	Required	Expansion of well-established avenues of research
Idea Award	Not required (can be included if available)	Novel, challenging existing paradigms; high risk
New Investigator Award	Not required (can be included if available)	To prepare new, independent investigators (Assistant Professor or equivalent with no more than 6 years of experience in the field of NF) and attract more senior investigators new to the NF field

Approximately $2M will be available for Idea Awards. Funding for Idea Awards can be requested for an average of $100,000 per year in direct costs, for a maximum of $200,000 over 2 years, plus indirect costs as appropriate. Funds can be requested for salary, expenses including

research supplies, and travel to scientific meetings. Budget is a key consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. No more than one trip to a scientific meeting per award per year is funded.

Applicants may not submit the same proposal to more than one of the following categories: Idea Awards (Section III); New Investigator Awards (Section IV); Investigator-Initiated Research Awards (Section V); or Clinical Trial Awards (Section VI).

III-B. Scientific Peer Review – Evaluation for Idea Award

Idea 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? Does the applicant acknowledge potential problem areas and consider alternative methods/tactics? Preliminary data are not required but may be included. If included, do the preliminary data support the scientific rationale for the study? Does the investigator provide limited preliminary data or a clear-cut rationale supporting the research strategy?

- **Innovation:** Does the research employ novel concepts, approaches, or methods? Are the aims original and innovative? Does the project challenge existing paradigms, develop new methodologies or technologies, or address under-explored or unexplored areas?

- **Scientific Relevance and Impact:** Does this study address a critical problem in NF research? What will be the effect of these studies on the concepts or methods that drive this field? Does the proposal make a convincing case for the relevance of the research to NF? To what extent will the project, if successful, make an original and important contribution to the goal of ameliorating the effects of NF?

- **Principal Investigator:** Is the Principal Investigator (PI) appropriately trained and well suited to carry out this work? Is the proposed work appropriate to the experience level of the PI and other researchers (if any)? Is there appropriate representation from all the expertise areas needed to conduct the study successfully?

- **Environment:** Is the scientific environment an appropriate setting for the proposed research? Are the research requirements adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed? Is there evidence of institutional support?

- **Budget:** Is the budget reasonable for the research proposed? Are arrangements made to compensate human subjects/participants for expenses they incur from participating in the project where appropriate?

III-C. Programmatic Review – Evaluation Criteria for Idea Award Proposals

Funding recommendations at the second tier of review, programmatic review, are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. Additional details on programmatic review procedures and evaluation criteria are included in Section I-B.2.

III-D. Letter of Intent

All applicants considering submission of a proposal in response to this Program Announcement are requested to submit a "Letter of Intent" form as soon as possible. This form can be found in Appendix A, or it can be completed online at the CDMRP website (*http://cdmrp.army.mil*). Please fax, e-mail, or mail the "Letter of Intent" form to:

Fax: (301) 682-5521
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP99-Announcement)
524 Palacky Street
Fort Detrick, MD 21702-5024

III-E. Proposal Preparation

The following proposal preparation information is specific for the Idea Award mechanism. Please note that the body of the proposal is limited to 10 pages, inclusive of figures, tables and graphs, and that the deadline for receipt is **September 15, 1999 at 4:00 p.m. Eastern Time**. Proposed start dates should be no earlier than June 1, 2000 and no later than September 30, 2000.

1. Who May Apply – See Appendix C, part 1.

2. Proposal Acceptance Criteria – See Appendix C, part 2.

3. Proposal Cover Booklet – See Appendix C, part 3.

4. Peer Review Referral Page – See Appendix C, part 4.

5. Proposal Title Page – See Appendix C, part 5.

6. Table of Contents – See Appendix C, part 6.
   Use the table of contents shown below in your proposal submission. As listed, number all pages consecutively at the bottom center, beginning with the Proposal Title Page.

Idea Award
Table of Contents

7. Proposal Abstracts – See Appendix C, part 7.

8. Statement of Work – See Appendix C, part 8.

9. Proposal Relevance and Impact Statement – See Appendix C, part 9.
   In addition, as part of the Proposal Relevance and Impact Statement, Idea Award applicants should explicitly state how the proposal will have an impact upon and further the programmatic goals.

10. Proposal Body – See Appendix C, part 10.
    The body of Idea Award proposals is limited to 10 pages inclusive of figures, tables, and graphs. Submission of color figures, tables, graphs, or photographs is not recommended (see Appendix C, part 2).

    For Idea Award proposals, it is the responsibility of the investigator to clearly articulate how the proposed research is innovative. Presentation of preliminary or pilot data is not required for Idea Awards, but can be included if available. In addition, the applicant should describe the proposed project using the **general** outline provided below:

a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to the proposal. Cite relevant literature references.

b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

c. Objectives: State concisely the specific aims of the study.

d. Methods: Give details about the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation. All figures, tables, and diagrams must be included within the proposal body.

Applicants should consider the peer and programmatic review evaluation criteria when writing the body of the proposal.

11. References – See Appendix C, part 11.

12. Biographical Sketches – See Appendix C, part 12.

13. Existing/Pending Support – See Appendix C, part 13.

14. Facilities/Equipment Description – See Appendix C, part 14.

15. Support Documentation – See Appendix C, part 15.
    A letter of institutional support and commitment, demonstrating availability of laboratory facilities, equipment, and intent to foster the applicant's research career is required.

16. Detailed Cost Estimate – See Appendix C, part 16.

17. Instruments – See Appendix C, part 17.

18. Publications and Patent Abstracts – See Appendix C, part 18.

19. Proposal Submission – See Appendix C, part 19.

20. Submission Deadline – See Appendix C, part 20.
    The deadline for receipt of Idea Award proposals is **September 15, 1999 at 4:00 p.m. Eastern Time**.

21. Appendices – See Appendix C, part 21.

22. Notification – See Appendix C, part 22.

III-F. Reports

Timely submission of progress reports is a requirement of the USAMRMC. The PIs of Idea Awards should plan on a requirement that consists of:

1. an **ANNUAL** report (for each year of research except the final year) that presents a detailed summary of findings (positive and negative), scientific issues, and accomplishments; and

2. a **FINAL** report (submitted in the last year of the grant period) that details the findings and accomplishments for the entire project.

The USAMRMC will notify PIs when these reports are due and provide format guidelines at that time. Additionally, all awardees will be required to enter research progress and accomplishments into a Government-provided software program.

All investigators are strongly encouraged to publish their results in the scientific literature. All publications, abstracts, and presentations must cite the DOD as the source of research funding. PIs must submit a copy of any manuscripts or publications resulting from their research to the USAMRMC. Furthermore, investigators who contemplate filing licensing agreements or patent applications arising from the research funded by the DOD must contact their USAMRMC contract specialist for guidance.

IV. New Investigator Awards

IV-A. New Investigator Awards

The intent of NIAs is to prepare new, independent investigators (Assistant Professor or equivalent with no more than 6 years of experience in the field of NF) for careers in NF and to present an opportunity to attract established investigators new to the NF field. The PI is required to submit several items of support documentation: a completed Statement of Eligibility form, a letter of institutional support and commitment, and letters of recommendation (one from a previous supervisor or mentor and one from the current head of the department) (see Section IV-E, item 15). The research focus of NIA proposals should address an issue relevant to NF. In accordance with the challenge to be innovative, **proposals lacking pilot data will be accepted if they demonstrate solid scientific judgment**. The proposed studies may be untested, but with a high probability of revealing new avenues of investigation. Although this research is inherently risky in nature and does not require preliminary or pilot data, these proposals nonetheless should be based on a sound scientific rationale that is established through a critical review and analysis of the literature and/or logical reasoning. Table IV-1 delineates the differences between traditional research, Idea Award proposals, and NIA proposals.

Table IV-1: Differences between Traditional Research Proposals, Idea Award Proposals, and New Investigator Award Proposals

Type of Proposal	Preliminary or Pilot Data	Description of Award Mechanism
Traditional Research	Required	Expansion of well-established avenues of research
Idea Award	Not required (can be included if available)	Novel, challenging existing paradigms, high risk
New Investigator Award	Not required (can be included if available)	To prepare new, independent investigators (Assistant Professor or equivalent with no more than 6 years of experience in the field of NF) and attract more senior investigators new to the NF field

Approximately $2M will be available for NIAs. Funding for NIAs can be requested for an average of $100,000 per year in direct costs for a maximum of $300,000 over 3 years plus indirect costs as appropriate. Funds can be requested for salary, expenses including research supplies, and travel to scientific meetings. Budget is a key consideration in both peer and programmatic review; applicants are cautioned to use discretion in budget requests. No more than one trip to a scientific meeting per award per year is funded.

Applicants may not submit the same proposal to more than one of the following categories: Idea Awards (Section III); New Investigator Awards (Section IV); Investigator-Initiated Research Awards (Section V); or Clinical Trial Awards (Section VI).

IV-B. Scientific Peer Review Evaluation for New Investigator Awards

NIA 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? Does the applicant acknowledge potential problem areas and consider alternative methods/tactics? Preliminary data are not required but may be included. If included, do the preliminary data support the scientific rationale for the study? Does the investigator provide limited preliminary data or a clear-cut rationale supporting the research strategy?

- **Innovation:** Does the research employ novel concepts, approaches, or methods? Are the aims original and innovative? Does the project challenge existing paradigms, develop new methodologies or technologies, or address underexplored or unexplored areas?

- **Scientific Relevance and Impact:** What will be the effect of these studies on the concepts or methods that drive this field? To what extent will the project, if successful, make an original and important contribution? Does this study address a critical problem in NF research? Does the proposal make a convincing case for the relevance of the research to NF?

- **Principal Investigator:** Is the PI appropriately trained and well suited to carry out this work? Does the PI show potential for contribution to the NF field? Is the proposed work appropriate to the experience level of the PI and other researchers (if any)? Is there appropriate representation from all the expertise areas needed to conduct the study successfully?

- **Environment:** Is the scientific environment an appropriate setting for the proposed research? Are the research requirements adequately supported by the scientific environment, necessary resources, and any collaborative arrangements proposed? Is there evidence of institutional support? Does the institutional letter of support describe adequate support for the applicant's career development through this proposal?

- **Budget:** Is the budget reasonable for the research proposed? Are arrangements made to compensate human subjects/participants for expenses they incur from participating in the project where appropriate?

IV-C. Programmatic Review – Evaluation Criteria for NIA Proposals

Funding recommendations at the second tier of review, programmatic review, are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. Additional details on programmatic review procedures and evaluation criteria are included in Section I-B.2.

IV-D. Letter of Intent

All applicants considering submission of a proposal in response to this Program Announcement are requested to submit a "Letter of Intent" form as soon as possible. This form can be found in Appendix A, or it can be downloaded from the USAMRMC Congressionally Directed Medical Research Programs website (*http://cdmrp.army.mil*). Please fax, e-mail, or mail the "Letter of Intent" form to:

Fax:	(301) 682-5521
E-mail:	cdmrp.pa@det.amedd.army.mil
Mail:	Commander, U.S. Army Medical Research and Materiel Command ATTN: MCMR-PLF (NFRP99-Announcement) 524 Palacky Street Fort Detrick, MD 21702-5024

IV-E. Proposal Preparation

The following proposal preparation information is specific for the NIA category. Specific instructions for proposal preparation are found in Appendix C of this Program Announcement. Please keep in mind that a requirement of the NIA category is that the principal investigator be an independent investigator (Assistant Professor or equivalent with no more than 6 years experience in the field of NF) *or* a more senior investigator new to the field. The Statement of Eligibility form found at the end of this subsection must be completed and submitted with the proposal. In addition, please note that the body of the proposal is limited to 15 pages and that the deadline for submission is **September 15, 1999 at 4:00 p.m. Eastern Time**. Proposal start dates should be no earlier than June 1, 2000 and no later than September 30, 2000.

1. Who May Apply – See Appendix C, part 1.

2. Proposal Acceptance Criteria – See Appendix C, part 2.

3. Proposal Cover Booklet – See Appendix C, part 3.

4. Peer Review Referral Page – See Appendix C, part 4.

5. Proposal Title Page – See Appendix C, part 5.

6. Table of Contents – See Appendix C, part 6.
   Use the table of contents shown below in your proposal submission. As listed, number all pages consecutively at the bottom center, beginning with the Proposal Title Page.

New Investigator Award
Table of Contents

Page Number

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7. Proposal Abstracts – See Appendix C, part 7.

8. Statement of Work – See Appendix C, part 8.

9. Proposal Relevance and Impact Statement – See Appendix C, part 9.
   In addition, as part of the Proposal Relevance and Impact Statement, NIA applicants should explicitly state how the proposal will have an impact upon and further the programmatic goals.

10. Proposal Body – See Appendix C, part 10.
    The body of NIA proposals is limited to 15 pages inclusive of figures, tables, and graphs. Submission of color figures, tables, graphs, or photographs is not recommended (see Appendix C, part 2). Presentation of preliminary or pilot data is not required for NIAs but can be included if available. In addition, the PI should describe the proposed project using the **general** outline provided below:

    a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to this proposal. Cite relevant literature references.

    b. Hypothesis/Purpose: State the hypothesis to be tested and the expected results.

    c. Objectives: State concisely the specific aims of the study.

    d. Methods: Give details about the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation. All figures, tables, and diagrams must be included within the proposal body.

    Applicants should consider the peer and programmatic review evaluation criteria when writing the body of the proposal.

11. References – See Appendix C, part 11.

12. Biographical Sketches – See Appendix C, part 12.

13. Existing/Pending Support – See Appendix C, part 13.

14. Facilities/Equipment Description – See Appendix C, part 14.

15. Support Documentation – See Appendix C, part 15.
    In addition to the instructions found in Appendix C, part 15, applicants for an NIA must submit a form signed by the Department Chair, Dean, or equivalent official indicating that the PI is an independent investigator (Assistant Professor or equivalent with no more than 6 years experience in the field of NF) *or* a more senior investigator new to the field and, therefore, an eligible applicant for this award type. The Statement of Eligibility form at the end of this subsection should be used.

    A letter of institutional support must also be included in this section. The letter shall include a discussion of the level of institutional commitment to foster the applicant's research career as reflected by (1) the extent to which the applicant will be relieved of his or her academic responsibilities to have additional time for research, (2) the provision of adequate laboratory facilities and equipment, and (3) the opportunities for critical

professional interaction with senior colleagues. In addition, the applicant must submit a letter of recommendation from (a) a previous supervisor or mentor and (b) the current head of the department.

16. Detailed Cost Estimate – See Appendix C, part 16.

17. Instruments – See Appendix C, part 17.

18. Publications and Patent Abstracts – See Appendix C, part 18.

19. Proposal Submission – See Appendix C, part 19.

20. Submission Deadline – See Appendix C, part 20.
    The deadline for receipt of NIA proposals is **September 15, 1999 at 4:00 p.m. Eastern Time.**

21. Appendices – See Appendix C, part 21.

22. Notification – See Appendix C, part 22.

STATEMENT OF ELIGIBILITY

Name of Applicant:_____

Title of Proposal:_____

Name of Applicant's Organization:_____

Location of Applicant's Organization:_____

_____

Signature of Applicant:_____

STATEMENT OF ELIGIBILITY

For the purposes of the Department of Defense Congressionally Directed Medical Research Programs' Neurofibromatosis Research Program New Investigator Award category as outlined in the Announcement, the applicant fulfills all of the following criteria:

- holds a position of Assistant Professor or equivalent with no more than 6 years experience in the field of NF

OR

- is a more senior investigator new to the field;

AND

- has his/her own independent research facilities;

I, _____of _____
(printed name of Department Chair, Dean or equivalent official) (printed name of institution)
attest that the above-named investigator fulfills the requirements for a New Investigator Award.

Signature of Official_____ Date:_____

IV-F. Reports

Timely submission of progress reports is a requirement of the USAMRMC. The PIs of NIAs should plan on a requirement that consists 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 grant period) that details the findings and issues for the entire project.

The USAMRMC will notify PIs when these reports are due and provide format guidelines at that time. Additionally, all awardees will be required to enter research progress and accomplishments into a Government-provided software program.

All investigators are strongly encouraged to publish their results in the scientific literature. All publications, abstracts, and presentations must cite the DOD as the source of the research funding. PIs must submit a copy of any manuscripts or publications resulting from their research to the USAMRMC. Furthermore, investigators who contemplate filing licensing agreements or patent applications arising from the research funded by DOD must contact their contracting specialist and must follow the instructions concerning such activity in their contract.

V. Investigator-Initiated Research Awards

V-A. Investigator-Initiated Research Awards

The intent of IIRAs is to sponsor basic research leading to clinical trials relevant to NF. These grants are intended to fund independent investigators (at least Assistant Professor or equivalent) across a broad spectrum of disciplines for up to 3 years. A letter demonstrating strong institutional support for the project must be included . If a Nested Post-doctoral Traineeship is included in the proposal, the letter of institutional support must show evidence of support of the training program. (See Section V-E, item 15.)

Programmatic interests include proposals that:

- perform cellular and biochemical studies investigating how abnormal functions of NF1 and NF2 lead to pathogenesis;
- perform studies of normal, cellular biological functions of NF1 and NF2 proteins in a variety of cell types, not necessarily nor exclusively the disease target tissue;
- expand the knowledge of the genes that contribute to NF beyond the Gap-related domain in NF1;
- are aimed at defining the genetic and non-genetic factors that play a role in tumor formation, growth, and progression in NF1 and NF2 tumors;
- focus on how NF1 and NF2 protein function or lack of function leads to pathogenesis;
- study the effect of hormonal events on tumor growth;
- focus on the development of improved models for gene therapy, especially for NF2;
- emphasize the use of existing model systems to test potential therapies;
- develop new methods of imaging and measurement of lesions including new approaches to quantitation of dermal NF;
- study the pathogenesis of pseudoarthrosis and bone abnormalities in NF1; and
- address early childhood developmental, psychosocial, and cognitive aspects for NF1.

The allocation for IIRAs, with or without Nested Post-doctoral Traineeships, is approximately $3M. Although there are no total dollar amount restrictions to these awards, funding for IIRAs can be requested for up to 3 years only. Budget is a key consideration in both peer and programmatic review, and applicants are cautioned to use discretion on budget requests. In addition, ***applicants must include preliminary data to support the feasibility of the proposed research hypotheses and scientific approach.*** A clear experimental and statistical plan should be included as part of the proposal.

Nested Post-doctoral Traineeships are being offered as an optional part of IIRA proposals. The intent of these Nested Post-doctoral Traineeships 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 an IIRA proposal. Nested Post-doctoral Traineeships can be requested for a maximum of $48,000 per year inclusive of direct and indirect costs for a maximum of $144,000 per trainee over 3 years.

There is no limit to the number of post-doctoral traineeships nested under a given IIRA proposal. Expenses relevant to the traineeship(s) should be listed under the "Other" category on the "Detailed Cost Estimate."

Because post-doctoral traineeships will be nested within the IIRA, no post-doctoral trainees will be funded as regular salaried employees. It is requested that indirect charges related to the fellowships be at the lowest possible rates. An institutional post-doctoral traineeship must be requested for each proposed post-doctoral candidate.

To Be Named (TBN) trainees are acceptable for the proposal. Named post-doctoral candidates, however, should submit a biographical sketch of no more than three pages and include it in the biographical sketch section (see Appendix C, part 12). When TBN trainees are ultimately selected, the USAMRMC must be notified and the name and biographical sketch of each candidate must be provided.

Budget is a key consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. Funds for IIRA Proposals and Nested Post-doctoral Traineeships may be requested for faculty salary, student stipends, seminars and courses, administrative support (e.g., photocopying charges, telephone and fax services, secretarial support, etc.), and travel to scientific meetings. For the PI, no more than one trip to a scientific meeting per award per year is funded. Post-doctoral trainees may also attend one scientific meeting per year.

Applicants may not submit the same proposal to more than one of the following categories: Idea Awards (Section III); New Investigator Awards (Section IV); Investigator-Initiated Research Awards (Section V); or Clinical Trial Awards (Section VI).

V-B. Scientific Peer Review – Evaluation Criteria for Investigator-Initiated Research Awards

IIRA proposals will be evaluated according to the following criteria:

- **Research Strategy:** Is the scientific and technical merit of the proposed research clearly outlined in the conceptual framework, hypotheses, design, methods, and statistical analyses? Have potential problems been identified and reasonable solutions proposed? Does the research employ novel concepts, approaches, and methods?

- **Scientific Relevance and Impact:** What is the potential impact of the proposed research on the study of NF? Does the proposed work address a critical problem in NF research? Does the proposed effort have the potential to affect significantly the concepts or methods that are central to progress in NF research? To what extent will the work make an original and significant contribution?

- **Personnel:** Is the PI appropriately trained and well suited to carry out this work? Are the scientific personnel, other than the PI, well qualified to participate in the project? Are the other scientific personnel and faculty well qualified to participate in this project and conduct training for post-doctoral trainees, if included? Is there a senior staff member who is identified and responsible for each post-doctoral trainee?

- **Environment and Resources:** Is the scientific environment an appropriate setting for the proposed research? Is there a strong institutional commitment to NF research, evidenced by an institutional letter of support for the project, including support for training (for proposals with a Nested Post-doctoral Traineeship) in the support documentation? Are the necessary resources present to conduct the research? If not, are collaborative arrangements proposed?

- **Budget:** Is the budget reasonable for the research proposed? Are Nested Post-doctoral Trainees included with a stipend and expenses, and not as salaried personnel? Are arrangements made to compensate human subjects/participants for expenses they incur from participating in the project where appropriate?

V-C. Programmatic Review – Evaluation Criteria for Investigator-Initiated Research Award Proposals

Funding recommendations at the second tier of review, programmatic review, are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. Additional details on programmatic review procedures and evaluation criteria are included in Section I-B.2.

V-D. Letter of Intent

All applicants considering submission of a proposal in response to this Program Announcement are requested to submit a "Letter of Intent" form as soon as possible. This form can be found in Appendix A, or it can be downloaded from the CDMRP website (*http://cdmrp.army.mil*). Please fax, e-mail, or mail the "Letter of Intent" form to:

Fax:	(301) 682-5521
E-mail:	cdmrp.pa@det.amedd.army.mil
Mail:	Commander, U.S. Army Medical Research and Materiel Command ATTN: MCMR-PLF (NFRP99-Announcement) 524 Palacky Street Fort Detrick, MD 21702-5024

V-E. Proposal Preparation

The following proposal preparation information is specific for the IIRA mechanism. Please note that the body of the proposal is limited to 20 pages and that the deadline for receipt is **September 15, 1999 at 4:00 p.m. Eastern Time**. Proposed start dates should be no earlier than June 1, 2000 and no later than September 30, 2000.

1. Who May Apply – See Appendix C, part 1.

2. Proposal Acceptance Criteria – See Appendix C, part 2.

3. Proposal Cover Booklet – See Appendix C, part 3.

4. Peer Review Referral Page – See Appendix C, part 4.

5. Proposal Title Page – See Appendix C, part 5.

6. Table of Contents – See Appendix C, part 6.
   Use the table of contents shown below in your proposal submission. As listed, number all pages consecutively at the bottom center, beginning with the Proposal Title Page.

Investigator-Initiated Research Award
Table of Contents

Page Number

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7. Proposal Abstracts – See Appendix C, part 7.

8. Statement of Work – See Appendix C, part 8.

9. Proposal Relevance and Impact Statement – See Appendix C, part 9.
   In addition, as part of the Proposal Relevance and Impact Statement, IIRA applicants should explicitly state how the proposal will have an impact upon and further the programmatic goals.

10. Proposal Body – See Appendix C, part 10.
    The body of IIRA proposals is limited to 20 pages inclusive of figures, tables, and graphs. Submission of color figures, tables, graphs, or photographs is not recommended (see Appendix C, part 2).

    The inclusion of preliminary data is required for IIRA proposals. Applicants should include preliminary data to support the feasibility of the proposed research hypotheses and scientific approach. In addition, the PI should describe the proposed project using the **general** outline provided below:

    a. Background: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to the proposal. Cite relevant literature references.

    b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested and the expected results.

    c. Objectives: State concisely the specific aims of the study.

    d. Methods: Give details about the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation. All figures, tables, and diagrams must be included within the proposal body.

    Applicants should consider the peer and programmatic review evaluation criteria when writing the body of the proposal.

11. References – See Appendix C, part 11.

12. Biographical Sketches – See Appendix C, part 12.
    In addition to the required biographical sketches from the PI and other key investigators, a biographical sketch of no more than three pages should be included in this section for each named post-doctoral candidate.

13. Existing/Pending Support – See Appendix C, part 13.

14. Facilities/Equipment Description – See Appendix C, part 14.

15. Support Documentation – See Appendix C, part 15.
    A letter demonstrating strong institutional support for the project must be included. If a Nested Post-doctoral Traineeship is included in the proposal, the letter of institutional support must show evidence of support of the training program. (See Section V-E, item 15.)

16. Detailed Cost Estimate – See Appendix C, part 16.
    Note that expenses relevant to the post-doctoral traineeship should be listed under the "Other" category in the Detailed Cost Estimate.

17. Instruments – See Appendix C, part 17.

18. Publications and Patent Abstracts – See Appendix C, part 18.

19. Proposal Submission – See Appendix C, part 19.

20. Submission Deadline – See Appendix C, part 20.
    The deadline for receipt of IIRA proposals is **September 15, 1999 at 4:00 p.m. Eastern Time**.

21. Appendices – See Appendix C, part 21.

22. Notification – See Appendix C, part 22.

V-F. Reports

Timely submission of progress reports is a requirement of the USAMRMC. The PIs of IIRAs should plan on a requirement that consists of:

- an **ANNUAL** report (for each year of research except the final year) that presents a detailed summary of findings (positive and negative), scientific issues, and accomplishments; and

- a **FINAL** report (submitted in the last year of the grant period) that details the findings and accomplishments for the entire project.

The USAMRMC will notify PIs when these reports are due and provide format guidelines at that time. Additionally, all awardees will be required to enter research progress and accomplishments into a Government-provided software program.

All investigators are strongly encouraged to publish their results in scientific literature. All publications, abstracts, and presentations must cite the DOD as the source of research funding. PIs must submit a copy of any manuscripts or publications resulting from their research to the USAMRMC. Furthermore, investigators who contemplate filing licensing agreements or patent applications arising from the research funded by the DOD must contact their USAMRMC contract specialist for guidance.

VI. Clinical Trial Awards

VI-A. Clinical Trial Awards

The intent of CTAs is to sponsor clinical pharmacologic or gene therapy studies that look at toxicities (Phase 1) or investigate the efficacy (Phase 2) of any novel therapeutic approach for NF1 or NF2. CTAs will support Phase 1 and Phase 2 clinical trials that are likely to have a major impact on the treatment of NF. Ultimately, the goal of the CTA category is to sponsor novel research that will result in substantial improvements over today's approach to the treatment of NF. The USAMRMC's Office of the CDMRP is currently soliciting the submission of CTA proposals from investigators with expertise in NF and experience in conducting clinical trials.

Applicants must include preliminary data to support the feasibility of their hypotheses and approaches, along with a detailed plan to conduct a Phase 1 or 2 clinical trial during the course of the award. A requirement for consideration will be the inclusion of a clear experimental and appropriately powered statistical plan. ***Inquiry Review Panel (IRB) approval and informed consent form from at least one participating institution must be submitted with the proposal by the receipt deadline (September 15, 1999 at 4:00 p.m. Eastern Time).***

Up to $3M are available for CTAs. There are no dollar amount restrictions to these awards. Up to 3 years of funding may be requested. Clinical trials often require the collaboration of multiple centers to assure sufficient patient access. Proposals that involve such collaborations should describe the role of each collaborating center in the clinical trial. Additionally, separate budget justifications (see Appendix C, part 16), and facilities/equipment description (see Appendix C, part 14) should be submitted for each center, and commitment from the principal investigators and their respective institutions should be provided as support documentation (see Appendix C, part 15). Budget is a key consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. As noted in Appendix L, it is the policy of the DOD that the equipment needed to support proposed research will be provided only in rare cases. The focus of the CTA should be on the clinical trial. Therefore, careful consideration will be given to the appropriate percentage of the budget that will be devoted to equipment/ infrastructure. No more than one trip to a scientific meeting per award per year is funded.

Applicants may not submit the same proposal to more than one of the following categories: Idea Awards (Section III); New Investigator Awards (Section IV); Investigator-Initiated Research Awards (Section V); or Clinical Trial Awards (Section VI).

VI-B. Peer Review Evaluation Criteria – Clinical Trial Awards

CTA proposals will be evaluated according to the following criteria:

- **Trial Design:** Are the conceptual framework, design, methods, and analyses adequately developed and well integrated, including laboratory and other preclinical evidence, to support the clinical feasibility and promise of the approach? Have the logistical aspects of the clinical trial been appropriately addressed? Does the applicant demonstrate sufficient patient accrual? Has the availability of subjects for the trial, the prospect of their participation, and the likelihood of subject attrition been addressed? Is the recruitment schedule reasonable?

- **Clinical Relevance and Impact:** Does the study address an important problem related to the treatment of NF? If the aims of the application are achieved, are they likely to have a substantial clinical impact?

- **Statistical Plan:** Is the design of the clinical trial sound and sufficiently well developed with the required statistical power to lead to significant results? Is a clear statistical plan, including sample size projections and power analysis, outlined in the proposal? Is the appropriate statistical expertise represented on the research team?

- **Study Investigators:** Does the PI have expertise in NF and experience conducting clinical trials? Are the other scientific personnel well qualified to participate in the project? Is there representation from all the areas of expertise needed to conduct the clinical trial successfully?

- **Environment and Resources:** Are letters of commitment included from participating centers? Are there assurances that therapies to be used are available? Is there an appropriate clinical setting and are institutional resources available to support the study at each participating center?

- **Budget:** Is the budget reasonable for the research proposed? Are arrangements made to compensate human subjects/participants for expenses they incur from participating in the project where appropriate?

VI-C. Programmatic Review – Evaluation Criteria for CTA proposals

Funding recommendations at the second tier of review, programmatic review, are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. Additional details on programmatic review procedures and evaluation criteria are included in Section I-B.2.

VI-D. Letter of Intent

All applicants considering submission of a CTA proposal in response to this Program Announcement are requested to submit a "Letter of Intent" form as soon as possible. This form can be found in Appendix A, or it can be downloaded from the CDMRP website (*http://cdmrp.army.mil*). Please fax, e-mail, or mail the "Letter of Intent" form to:

Fax: (301) 682-5521
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP99-Announcement)
524 Palacky Street
Fort Detrick, MD 21702-5024

VI-E. Proposal Preparation

The following proposal preparation information is specific for the CTA mechanism. Please note that the body of the proposal is limited to 50 pages and that the deadline for receipt is **September 15, 1999 at 4:00 p.m. Eastern Time**. Proposed start dates should be no earlier than June 1, 2000 and no later than September 30, 2000.

1. Who May Apply – See Appendix C, part 1.

2. Proposal Acceptance Criteria – See Appendix C, part 2.

3. Proposal Cover Booklet – See Appendix C, part 3.

4. Peer Review Referral Page – See Appendix C, part 4.

5. Proposal Title Page – See Appendix C, part 5.

6. Table of Contents – See Appendix C, part 6.
   Use the table of contents shown below in your proposal submission. As listed, number all pages consecutively at the bottom center, beginning with the Proposal Title Page.

Clinical Trial Award
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Page Number

7. Proposal Abstracts – See Appendix C, part 7.

8. Statement of Work – See Appendix C, part 8.

9. Proposal Relevance and Impact Statement – See Appendix C, part 9.
   In addition, as part of the Proposal Relevance and Impact Statement, CTA applicants should explicitly state how the proposal will have an impact upon and further the programmatic goals.

10. Proposal Body – See Appendix C, part 10.
    The body of CTA proposals is limited to 50 pages inclusive of figures, tables, and graphs. Submission of color figures, tables, graphs, or photographs is not recommended (see Appendix C, part 2).

    Applicants should consider the peer and programmatic review evaluation criteria when writing the body of the proposal. In addition, the applicant should describe the proposed project using the **general** outline provided below:

a. Background/Significance/Rationale: Provide a brief statement of the ideas and reasoning behind the proposed work. Describe previous experience most pertinent to the proposal, provide an overview of the state of the science, and discuss the current status and relevance of the trial. Cite relevant literature references as appropriate. State the significance and rationale of the proposed work.

b. Preliminary Studies: A presentation of the studies that led to the proposed clinical trial is required. Data from pilot studies and additional supporting data from other research that support the necessity, feasibility, and potentiality of the trial should also be provided.

c. Objectives: State the purpose and specific aims of the proposed study. Note that the specific aims must clearly delineate the primary and secondary endpoints to be measured.

d. Clinical Protocol:

   i. Study design for the intervention(s) to be used.
   ii. Discussion of the potential biases in the research protocol and how they will be addressed.
   iii. Description of clinical, behavioral, laboratory, and physiological tests and protocols.
   iv. Patient recruitment:
      a. Inclusion and exclusion criteria.
      b. Description of the criteria to be used for assignment of patients to experimental conditions, methods of randomization (if any), and study endpoints.
      c. Availability of patients.
      d. Characteristics and appropriateness of the study population.
      e. Approaches to be utilized for recruitment, retention, and follow-up.
      f. Plans for maintaining the cooperation of subjects and addressing composition changes in the study population over the course of the trial.
      g. Data supporting recruitment and retention estimates.
      h. Ability of clinical centers to recruit and retain the proposed number of subjects.
   v. Data management/quality control/data analysis.
      a. Approach to data management.
      b. Statistical plan including sample size calculations.
      c. Methods for monitoring quality and consistency of the intervention(s) and data collection.
   vi. Description of the methods of analysis (primary and secondary endpoints should be clearly defined and related to the power calculation).

vii. Human Subjects: The applicant should address any issues that may lead to concern for the welfare of subjects. The investigator must also address data security measures and confidentiality. IRB approval and informed consent form from at least one participating institution must be submitted with the proposal under Support Documentation by the receipt deadline **(September 15, 1999 at 4:00 p.m. Eastern Time.**

viii. Study organization/administration: A description of how the study will be organized and managed must be provided. Additionally, the following descriptions must also be included in the proposal body:
   a. Organizational chart showing the interactions between the PI, key personnel, and consumer representatives.
   b. Coordination of all participating centers.
   c. A timetable for completion of the various stages of the proposed clinical trial.

11. References – See Appendix C, part 11.

12. Biographical Sketches – See Appendix C, part 12.
    The Phase 1 or Phase 2 clinical trial must be directed by an investigator with experience in the conduct of clinical trials.

13. Existing/Pending Support – See Appendix C, part 13.

14. Facilities/Equipment Description – See Appendix C, part 14.
    Clinical, data management, and laboratory facilities, as well as required equipment should be described in detail for all participating institutions.

15. Support Documentation – See Appendix C, part 15.
    IRB approval and informed consent form from at least one participating institution must be included in this section. Documentation of commitment from collaborating centers must also be included in this section.

16. Detailed Cost Estimate – See Appendix C, part 16.
    A budget for the entire trial and data analysis period must be provided. If some costs of the trial are to be funded through other sources, provide detailed information about these sources. Budgets should clearly delineate which portions are being requested for support by this program and which are to be supported by other sources. A total overall budget as well as itemized, individual budgets for each year of support requested must be prepared. If multiple centers are proposed or if any subcontract(s) for personnel or facilities exist, separate itemized budgets must be prepared for each year of the study.

17. Instruments – See Appendix C, part 17.
    Please note that for CTAs, the clinical protocol must be included in the body of the proposal and not under the Instruments section.

18. Publications and Patent Abstracts – See Appendix C, part 18.

19. Proposal Submission – See Appendix C, part 19.

20. Submission Deadline – See Appendix C, part 20.
    The deadline for receipt of CTA proposals is **September 15, 1999 at 4:00 p.m. Eastern Time.**

21. Appendices – See Appendix C, part 21.

22. Notification – See Appendix C, part 22.

VI-F. Reports

Timely submission of progress reports is a requirement of the USAMRMC. The PIs of CTAs should plan on a requirement that consists of:

1. an **ANNUAL** report (for each year of research except the final year) that presents a detailed summary of findings (positive and negative), scientific issues, and accomplishments; and

2. a **FINAL** report (submitted in the last year of the grant period) that details the findings and accomplishments for the entire project.

The USAMRMC will notify PIs when these reports are due and provide format guidelines at that time. Additionally, all awardees will be required to enter research progress and accomplishments into a Government-provided software program.

All investigators are strongly encouraged to publish their results in scientific literature. All publications, abstracts, and presentations must cite the DOD as the source of research funding. PIs must submit a copy of any manuscripts or publications resulting from their research to the USAMRMC. Furthermore, investigators who contemplate filing licensing agreements or patent applications arising from the research funded by the DOD must contact their USAMRMC contract specialist and follow instructions concerning such activity on their project.