DEPARTMENT OF DEFENSE

FISCAL YEAR 2002
NEUROFIBROMATOSIS RESEARCH PROGRAM
PROGRAM ANNOUNCEMENT

March 5, 2002

Headquarters, U.S. Army Medical Research and Materiel Command
MCMR-PLF, 1077 Patchel Street
Fort Detrick, Maryland 21702-5024

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Foreword

The U.S. Army Medical Research and Materiel Command (USAMRMC) has been directed to continue the Department of Defense (DOD) Neurofibromatosis Research Program (NFRP). The deadline, format, and other criteria specified for proposals in this DOD Fiscal Year 2002 (FY02) NFRP Program Announcement are based on program objectives, public needs, and regulatory guidance.

Specific information on the USAMRMC, U.S. Army Medical Research Acquisition Activity (USAMRAA), the Congressionally Directed Medical Research Programs (CDMRP), and the DOD NFRP can be obtained from the CDMRP web site at http://cdmrp.army.mil. A copy of this program announcement and associated forms also can be downloaded from the CDMRP web site (for information on completing the Proposal Information, see Section 6, page iii of this Foreword).

1. Highlights of Changes from the FY01 Program Announcement

- There is no paper submission; applicants are only required to submit their proposals electronically as a Portable Document Format (PDF) file through the Internet (electronic submission).

- The Electronic Proposal Cover Booklet is now called Proposal Information and can be found online at http://cdmrp.org/proposals. Please see Appendix C for more information.

- No paper copies of this Program Announcement will be supplied by the CDMRP. The document and its associated appendices can be downloaded from the CDMRP web site (http://cdmrp.army.mil).

- Margins for proposal preparation and acceptance have been changed to a minimum of 0.5-inch top, bottom, right, and 1-inch left. The print area must not exceed 7.0 x 10.0 inches (approximately 19.0 cm x 25.5 cm).

- A new award mechanism, the Career Development Award, is being offered. This award is intended to encourage established scientists or research clinicians who are currently working in areas other than neurofibromatosis to shift their focus to neurofibromatosis research.

- The Clinical Trial Award mechanism is no longer requesting proposals for Pilot clinical trials; only proposals for Phase 1 or 2 clinical trials may be submitted.

- The maximum period of performance for Investigator-Initiated Research Awards has been increased from 3 to 4 years.

- The Certificate of Environmental Compliance and Principal Investigator Safety Program Assurance documents have been incorporated into Appendix B and are due with the proposal submission; additional documents related to Regulatory Compliance and Quality (RCQ) issues will be available on the CDMRP web site by April 2002. You will be notified if you need to submit these additional RCQ documents to support your submission.

- All submissions to the NFRP that involve human subjects should provide medical care for research-related injuries at no cost to the subject. Investigators should plan on budgeting for such costs.

2. Who May Apply

Individuals, regardless of ethnicity, nationality, or citizenship status, may apply through an eligible institution. Eligible institutions include for-profit, non-profit, public, and private organizations. Examples include universities, colleges, hospitals, laboratories, companies, and agencies of local, state, and federal governments. Please refer to sections on individual mechanisms for additional eligibility criteria.

3. Submission Deadline

An electronic PDF version of your proposal, which will serve as the official proposal submission, must be uploaded/submitted through the Internet by an authorized Administrative Representative of the Sponsored Programs Office (or equivalent) of your organization no later than **11:59 p.m. (applicant's local time) June 4, 2002**. See Appendix B, part 22 and Appendix C for additional details. Applicants unfamiliar with the preparation and submission of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

4. Timeline

Electronic Letter of Intent:	As soon as possible but no later than May 21, 2002.
Proposal Submission Deadline:	**One electronic PDF version** of the proposal must be sent through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002.**
Peer Review:	July 2002
Request for RCQ Documents:	As early as July 2002
Programmatic Review:	September 2002
Notification:	Approximately 2 weeks after programmatic review
Award Date:	Between November 2002 and September 2003

5. Inquiries

Questions concerning the proposal format or required documentation can be addressed to the CDMRP at:

Phone: 301-619-7079
Fax: 301-619-7792
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP02)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

Applicants should submit questions regarding this program as early as possible. Every effort will be made to answer questions within 5 working days.

Help lines will be available by May 7, 2002 to answer specific questions regarding the preparation of proposals for electronic submission, or the process of electronic submission. The help line phone numbers will be provided on two CDMRP web sites: the CDMRP web site (http://cdmrp.army.mil) and the proposal submission web site (http://cdmrp.org/proposals). Alternately, help can be obtained by e-mail at help-proposals-cdmrp@cdmrp.org.

6. Proposal Submission

Applicants should refer to sections on individual award mechanisms and Appendix B for appropriate submission requirements.

Proposals will be submitted electronically at http://cdmrp.org/proposals. The web site will be available for proposal submission by May 7, 2002. An authorized Administrative Representative from the Sponsored Programs Office of the applicant's organization must submit one electronic PDF version of the proposal, which will count as the official proposal submission.

Several steps are critical for successful electronic submission of the applicant's proposal:

1. The applicant is required to submit Proposal Information (referred to last year as the Electronic Proposal Cover Booklet) online at http://cdmrp.org/proposals, to include the e-mail address of an Administrative Representative from the Sponsored Programs Office who is authorized to conduct negotiations on the applicant's behalf (see Appendix C). **The Proposal Information must be submitted prior to submission of the proposal. Applicants are encouraged to begin this part of the submission process early and submit their Proposal Information at least 2 weeks prior to the submission deadline.**

2. Once the applicant has submitted the Proposal Information, the Administrative Representative from the Sponsored Programs Office will receive an e-mail notification that the Proposal Information is ready for his or her review.

3. Applicants will need to provide the Administrative Representative with an electronic copy of the proposal. Applicants are encouraged to coordinate early with their Sponsored Programs Office.

4. The Administrative Representative is required to provide final approval of the Proposal Information and then to upload/submit the proposal file in PDF. Please note that the web site does not allow applicants to upload/submit their proposals directly. **Proposals may ONLY be uploaded/submitted by the Administrative Representative from the Sponsored Programs Office and this can be done ONLY after he or she has approved the Proposal Information.**

Please note that all proposals must be submitted electronically to this program; printed supplemental materials will not be accepted. Any supporting documentation that the applicant wishes to include with the proposal must be scanned and incorporated into the PDF file prior to upload/submission. The Proposal Information must be completed online and the PDF version of the proposal uploaded/submitted through the web site (http://cdmrp.org/proposals) no later than **11:59 p.m. (applicant's local time) June 4, 2002.** Detailed instructions for electronic submissions will be available at http://cdmrp.org/proposals no later than May 7, 2002.

I. Overview of the Congressionally Directed Medical Research Programs

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

Due to increased public awareness, the success of the Department of Defense (DOD) Congressionally Directed Medical Research Programs (CDMRP), and the work of grassroots advocacy organizations, Congress has appropriated monies for peer reviewed research directed toward specific diseases. Beginning in fiscal year 1992, the U.S. Congress has directed the DOD to manage these various extra- and intramural grant programs. The U.S. Army Medical Research and Materiel Command (USAMRMC) established the CDMRP to administer these funds. To date, the USAMRMC CDMRP has received more than $2.2 billion targeted by Congress for peer reviewed research on breast cancer, prostate cancer, ovarian cancer, neurofibromatosis, tuberous sclerosis, Defense Women's Health, osteoporosis, and other specified areas.

The CDMRP exists to support research that will positively impact the health of all Americans. The CDMRP strives to identify gaps in funding and provide opportunities that will enhance program research objectives without duplicating existing funding. To meet these goals, the CDMRP has developed unique mechanisms to facilitate the funding of quality research that addresses individual program objectives.

I-B. Investment Strategy

For each program, the CDMRP has developed and refined a flexible 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. For each program, an expert Integration Panel (IP) of scientists, clinicians, and consumer advocates is convened to deliberate issues and concerns unique to the program, establish an appropriate investment strategy, and perform programmatic review as described in Section I-C.2. Based upon this investment strategy, each program then uses a variety of award mechanisms to address the most urgent needs of the research community.

I-C. Proposal Evaluation

The CDMRP uses a two-tiered review process for proposal evaluation as recommended by the National Academy of Science's Institute of Medicine. The two tiers are fundamentally different. The first tier is a scientific 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-C.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 proposals, based upon the review criteria published for each award mechanism.

Scientific peer review panels are composed of a chair, scientific reviewers, consumer reviewers, and a nonvoting executive secretary. Selection of individuals as scientific reviewers is predicated upon their expertise as well as their varied levels of experience with scientific peer review. For the breast, prostate, and ovarian cancer research programs, consumer reviewers are cancer survivors and representatives of consumer advocacy organizations. For the neurofibromatosis research program, consumer reviewers are individuals with neurofibromatosis or their family members and representatives of consumer advocacy organizations. Consumer reviewers are nominated by an advocacy organization and are selected on the basis of their leadership skills, commitment to advocacy, and interest in science. Consumers augment the scientific peer review by bringing the patient perspective to the assessment of science and to the relevance of research.

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

The peer review summary statement is a product of scientific peer review. Each summary statement includes the investigator's structured technical abstract and lay (nontechnical) abstract (verbatim), 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. Summary statements are forwarded to the next stage of the review process, programmatic review.

I-C.2. Programmatic Review

The second tier is programmatic review. Programmatic review is accomplished by the IP, which is composed of scientists, clinicians, and consumer advocates. The 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. One of the functions of programmatic review is to select 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. IP members use the peer review summary statements, which include the proposal abstracts, to review proposals. The Statement of Work may also be reviewed at this level. However, the full proposal is not forwarded to programmatic review.

The IP is committed to funding a broad-based research portfolio. The ratings and evaluations of scientific peer review panels are primary factors in programmatic review; the IP also must consider other criteria to establish this portfolio. The criteria the IP will use to make funding recommendations are:

- Ratings and evaluations of the scientific peer review panels;
- Programmatic relevance;
- Relative 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 selected by the IP and recommended to the Commanding General, USAMRMC, for funding.

I-D. Notification

Following completion of the two-tiered evaluation process, every applicant will receive a letter indicating the award status of his or her proposal, along with the peer review summary statement. Letters will be sent as official information becomes available. Thus, not all investigators will be notified at the same time.

I-E. Negotiation of the Award

Award negotiation consists of discussions, reviews, and justifications of several critical issues, including those involving the U.S. Army Medical Research Acquisition Activity (USAMRAA) and Regulatory Compliance and Quality (RCQ). A Contract Specialist from the USAMRAA will contact the Administrative Representative who is authorized to negotiate contracts and grants at the applicant's institution. As part of the negotiation process, additional documentation and justifications relating to the proposed Statement of Work and associated budgets may be required.

Please note that the award start date will be determined during the negotiation process.

Concurrent with the USAMRAA discussions, RCQ will review the environmental compliance, safety plan, animal use, and human subjects/anatomical substance use documents to ensure that Army regulations are met. The Certificate of Environmental Compliance and Principal Investigator Safety Program Assurance documents are part of the proposal submission. The

Facility Safety Plan (if needed), Research Involving Animals, and Research Involving Human Subjects and/or Anatomical Substances documents will be requested in the applicant's notification letter. All documents related to RCQ should be available on the CDMRP web site (http://cdmrp.army.mil) by April 2002.

I-F. Human Use Requirements Unique to DOD-Funded Research

Important distinctions exist for research funded by the DOD that involves human subjects. In addition to local Institutional Review Board (IRB) approval to conduct research involving human subjects, a second, DOD review and approval is also required. The Human Subjects Research Review Board (HSRRB), administered by the USAMRMC RCQ Office, is responsible for conducting this second level of review. 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. **All research protocols involving human subjects and/or anatomical substances must be approved by both the appropriate local review board and by the HSRRB before awards are made and prior to initiation of the research protocol.**

Two requirements specific to DOD-funded research that the applicant must specifically address, if applicable, in the development of a research proposal for submission to the DOD are outlined below.

- Medical Care for Research-Related Injuries. For all DOD-funded research involving human subjects, medical care for research-related injuries must be provided at no cost to the subject. Many institutions and states provide for this medical care as part of their liability insurance. If not, investigators should plan on budgeting for such costs. The institution business office can assist applicants with budgeting for this requirement. See Appendix F, part 7 for more details.

- Intent to Benefit. An individual not legally competent to consent (e.g., minors) may not be enrolled in DOD-sponsored research unless the research is intended to benefit each and every subject enrolled in the study. Applicants 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. Therefore, the applicant should articulate how the research will benefit minors or other individuals who are not legally competent to consent and are part of the placebo arm of the study.

More information regarding research involving human subjects can be found in the RCQ Document, "Research Involving Human Subjects and/or Anatomical Substances," which will be available on the CDMRP web site (http://cdmrp.army.mil) by April 2002.

I-G. Annual and Final Reports

All awards will require the timely delivery of several reports during the research effort. These reports are necessary for the CDMRP to monitor progress and evaluate program outcomes.

The Principal Investigator (PI) should plan on a reporting requirement consisting 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.

I-H. Publications and Patents

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 the research funding. For example, "This research, under award number DAMD…, was supported by the Department of Defense Neurofibromatosis Research Program, which is managed by the U.S. Army Medical Research and Materiel Command." A PI must submit a copy of any manuscript or publication resulting from research funded under the award to the CDMRP.

In accordance with the Bayh-Dole Act (35 USC 200 et seq.[1]), title to inventions and patents resulting from such federally funded research may be held by the grantee or its collaborator, but the U.S. 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.

[1] Title 35, United States Code, Section 200 et seq.

II. Department of Defense Neurofibromatosis Research Program

II-A. History of the Neurofibromatosis Research Program

The Department of Defense (DOD) Neurofibromatosis Research Program (NFRP) was established in fiscal year 1996 (FY96) to promote research directed toward decreasing the impact of neurofibromatosis (NF). The ultimate goal of the NFRP is to develop effective therapies for NF1 and NF2. The DOD used the model established through recommendations from the Institute of Medicine for the U.S. Army Medical Research and Materiel Command's (USAMRMC's) Breast Cancer Research Program (BCRP) to establish the NFRP. Like the BCRP, the NFRP employs a two-tiered scientific review process that funds meritorious research that will positively impact those living with NF1 or NF2. The program's success has encouraged Congress to appropriate additional funds to the NFRP in subsequent years, culminating in a $21M appropriation for the FY02 NFRP.

The program history for FY96-01 appropriations of the NFRP is shown in Table II-1.

Table II-1: History of the DOD's Peer Reviewed NFRP

Program History	FY96-00	FY01[1]
NFRP-Managed Appropriations for Peer Reviewed Research	$52.3M	$17M
Number of Proposals Received	175	48
Number of Proposals Funded	65	~20
Percentage of Applications Recommended for Funding	37%	~42%
Number of Research Awards	63	~20
Number of Infrastructure Awards	2	N/A[2]

[1] Award negotiations will not be finalized until September 2002.
[2] Not applicable.

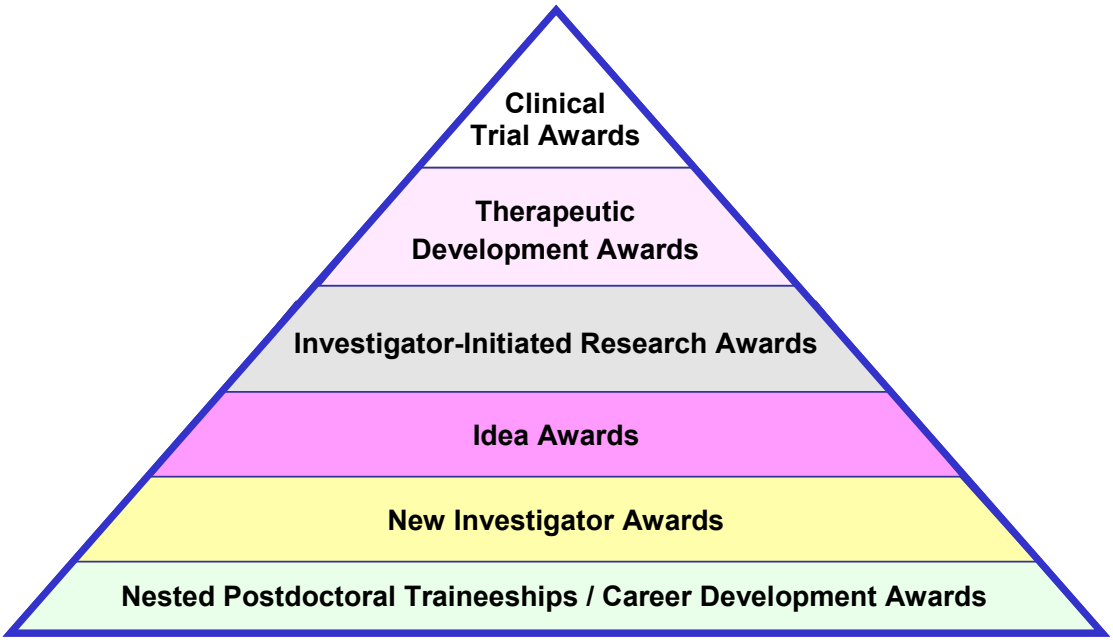
II-B. Overview of the FY02 NFRP

The Congressionally Directed Medical Research Programs (CDMRP) is requesting proposals on neurofibromatosis research and training through this program announcement. Proposals will be requested in six award mechanisms: New Investigator Awards, Idea Awards, Career Development Awards, Investigator-Initiated Research Awards (with optional Nested Postdoctoral Traineeships), Therapeutic Development Awards, and Clinical Trial Awards. The Career Development Award is new in FY02; details on this award mechanism can be found in Section V.

II-C. NFRP Emphasis Areas

The NFRP adapts the types of award mechanisms it offers each year to meet the current needs in NF research and treatment. Mechanisms are developed based upon recommendations of the CDMRP staff and Integration Panel, an expert panel of scientists, clinicians, and consumer advocates (Section I-B). Multiple factors are taken into consideration when designing and offering award mechanisms for each fiscal year. Award mechanisms offered each year complement and fill niches in research that are not offered/emphasized by other agencies. The overall funding philosophy of the NFRP is illustrated by the pyramid depicted in Figure II-1.

Figure II-1: FY02 NFRP Philosophy



The foundation of the pyramid is the training of investigators in NF research. The FY02 NFRP funds postdoctoral trainees as an optional part of Investigator-Initiated Research Awards (Section VI) and recruits mid-career scientists to NF research from other fields through Career Development Awards (Section V). At the second level of the pyramid, the NFRP funds junior investigators through New Investigator Awards (Section III). The third level of the pyramid is ideas. Research originates with thousands of ideas, not all of which will lead to fruitful areas of investigation. Idea Awards have been and continue to be a major emphasis of the NFRP (Section IV). At the fourth level of the pyramid, the NFRP funds both basic and clinically oriented NF research projects through Investigator-Initiated Research Awards (Section VI). Approaching the summit of the pyramid are Therapeutic Development Awards, which support the development and evaluation of preclinical model systems for NF (Section VII). At the pinnacle of the pyramid, the NFRP funds Phase 1 or 2 clinical trials with Clinical Trial Awards (Section VIII).

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 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.

II-D. FY02 NFRP Program Announcement Award Opportunities

This Command anticipates that $17.3M will be available to fund competitive, peer reviewed neurofibromatosis research proposals in two categories: (1) Training/Recruitment Awards and (2) Research Awards.

Allocations	**FY02**
Congressional Appropriation	$21.0M
Less: Congressional/DOD Withholds[1]	($2.2M)
Appropriation Received	$18.8M
Less: Approximate NFRP Management Costs[2]	($1.5M)
Amount Available for FY02 Research	$17.3M

[1]Withholds include Small Business Innovation Research (SBIR)/USAMRMC.
[2]Any cost savings from management cost will be applied to research funding.

Prospective applicants who are familiar with the CDMRP program requirements from previous years are urged to review this program announcement carefully because revisions have been made.

Important note regarding duplicate submissions: Submission of the same research project under different award mechanisms is **not** allowed, and all such duplicate submissions may be administratively withdrawn. This includes submissions under different award mechanisms from different Principal Investigators. However, an Idea Award may address the same research question proposed in a Career Development Award proposal; both proposals must specify the same Principal Investigator. The Government reserves the right to reject any proposal.

Reference Table of Award Mechanisms

Award Mechanism	Experience of Principal Investigator	Key Mechanism Elements	Dollars Available	Instructions for Proposal Preparation
New Investigator Awards	Independent investigators below the level of Associate Professor with access to appropriate research facilities	• Fund investigators in the early stages of their careers • Preliminary data not required	An average of $150,000 per year in direct costs for a maximum of $450,000 over 3 years, plus indirect costs as appropriate	Section III
Idea Awards	Independent investigators	• Fund innovative ideas and technology related to NF • Preliminary data not required	An average of $150,000 per year in direct costs for a maximum of $450,000 over 3 years, plus indirect costs as appropriate	Section IV
Career Development Awards	Independent investigators at a level equivalent to or above that of Associate Professor	• To relieve applicants from academic or clinical duties • Provides salary support; requires separate source of research support	An average of $60,000 per year for salary support and travel to scientific meetings for a maximum of $180,000 over 3 years, plus indirect costs as appropriate	Section V
Investigator-Initiated Research Awards (with optional Nested Postdoctoral Traineeship[s])	Independent investigators at a level equivalent to or above that of Assistant Professor Nested Postdoctoral Trainee: Recent doctoral graduates with 3 years or less of postdoctoral experience	• To sponsor basic and clinically oriented NF research • Preliminary data required	• No total dollar amount restrictions • Funding can be requested for up to 4 years • With Nested Postdoctoral Traineeship: a maximum of $60,000 per year inclusive of direct and indirect costs for a maximum of $240,000 per trainee over 4 years • No limit to the number of postdoctoral trainees nested under a given proposal	Section VI
Therapeutic Development Awards	Independent investigators	• To fund the development and evaluation of preclinical model systems for NF • To fund goal-focused, synergistic consortia	• No total dollar amount restrictions • Funding can be requested for up to 3 years	Section VII
Clinical Trial Awards	Independent investigators	• To fund Phase 1 or 2 clinical trials • Preclinical data required for all clinical trial proposals • Phase 1 or Pilot clinical trial data required for Phase 2 clinical trial proposals	• No total dollar amount restrictions • Funding can be requested for up to 3 years for Phase 1 clinical trials and for up to 4 years for Phase 2 clinical trials	Section VIII

III. New Investigator Awards

III-A. New Investigator Awards

The intent of New Investigator Awards is to help investigators at the early stages of their careers become established neurofibromatosis (NF) researchers (see Table III-1). To be eligible for this award, the applicant must be an independent investigator below the level of Associate Professor (or equivalent) with access to appropriate research facilities. The applicant is required to submit a completed Statement of Eligibility Form (see Section III-E, item 17). Please note that graduate students, postdoctoral fellows, and other "mentored" researchers are not eligible for these awards. Although New Investigator Award proposals do not require preliminary data, they should be based on a sound scientific rationale established through a critical review and analysis of the literature and/or logical reasoning.

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

Type of Proposal	Preliminary Data	Mechanism Purpose
New Investigator Award Proposal	Not required (can be included if available)	To prepare new, independent investigators below the level of Associate Professor
Idea Award Proposal	Not required (can be included if available)	To fund novel, high-risk research that challenges existing paradigms
Traditional Research Proposal	Required	To expand well-established avenues of research

Funding for New Investigator Awards can be requested for an average of $150,000 per year in direct costs for a maximum of $450,000 over 3 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. The amount allotted for travel is $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.

Submission of the same research project to the Fiscal Year 2002 (FY02) Neurofibromatosis Research Program (NFRP) under different award mechanisms is not allowed, and all such duplicate submissions may be administratively withdrawn. This includes submissions under different award mechanisms by different Principal Investigators (PIs). The Government reserves the right to reject any proposal.

III-B. Scientific Peer Review Evaluation Criteria for New Investigator Award Proposals

New Investigator Award proposals will be evaluated according to the following criteria:

- **Principal Investigator:** How well does the PI meet the goal of this award mechanism (i.e., is the PI relatively new to the field of NF research and below the level of Associate Professor or equivalent)? Does the PI show potential for contributing to the NF research field? Is the PI an independent (i.e., non-mentored) researcher? Is the proposed work appropriate to the experience level of the PI?

- **Relevance:** Does this study address a critical problem in NF research? To what extent will the project, if successful, make an original and important contribution to the goal of advancing research in the NF field? Does the proposal make a convincing case for the relevance of the research to NF?

- **Research Strategy:** Are the conceptual framework, hypotheses, design, methods, and analyses adequately developed and well integrated to the aims of the project? Are they based on sound scientific rationale and logical reasoning? Is there a clear-cut rationale supporting the research provided? 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?

- **Environment:** Is there evidence that the scientific environment is appropriate 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?

- **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?

III-C. Programmatic Review Evaluation Criteria for New Investigator Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the New Investigator Award mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

III-D. Letter of Intent

All applicants considering submission of a proposal in response to this program announcement are requested to submit an electronic Letter of Intent no later than May 21, 2002. This form is available on the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil/funding/02nfrp1

III-E. Proposal Preparation

Instructions for proposal preparation for all award mechanisms are found in Appendix B. The following supplemental information is specific for New Investigator Awards. Please note that the body of the proposal is limited to **10 pages**, inclusive of any figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn by the Government prior to peer review.** Applicants are required to submit the Proposal Information prior to upload/submission of the proposal. Ensure that one electronic Portable Document Format (PDF) version of your proposal, which will serve as the official proposal submission, is uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002.**

Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

1. Who May Apply – See Appendix B, part 1.
   Eligible applicants must be independent (i.e., non-mentored) investigators below the level of Associate Professor or equivalent with access to appropriate research facilities.

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

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Information – See Appendix B, part 4 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.

6. Table of Contents – See Appendix B, part 6.
   Use the table of contents found at on page III-6 in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8 and Appendix D.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.

11. Proposal Body – See Appendix B, part 11.
    The body of New Investigator Award proposals is limited to **10 pages**, inclusive of figures, tables, graphs, and photographs, if used. The inclusion of preliminary data is **not** required; however, investigators must demonstrate a sound scientific rationale established through a critical review and analysis of the literature and/or logical reasoning.

    Describe the proposed project using the general outline provided below:

    a. Background: Briefly describe the ideas behind the proposed work and cite relevant literature references. Describe previous experience most pertinent to this proposal.

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

    c. Objectives: State concisely the specific aims and the research strategy of the study.

    d. Methods: Describe the experimental design and methodology.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14 and Appendix E.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.

17. Administrative Documentation – See Appendix B, part 17.
    In addition to the documentation described in Appendix B, provide the following item in the Administrative Documentation section of the proposal submission.

    - A form signed by the Department Chair, Dean, or equivalent official verifying that the applicant is an independent investigator below the level of Associate Professor or equivalent with access to appropriate research facilities and therefore is an eligible applicant for this award type. Use the Statement of Eligibility Form on page III-7. This form must be signed and then scanned into the PDF file of your proposal prior to its submission to the CDMRP.

Proposals lacking required administrative documentation may be considered noncompliant and thus may not be forwarded for review (see Appendix B, part 21).

18. Detailed Cost Estimate – See Appendix B, part 18.
    Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. In addition, budgets will be reviewed during award negotiations. Please provide complete justification for expenses in all categories. Funding for New Investigator Awards can be requested for an average of $150,000 per year in direct costs for a maximum of $450,000 over 3 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. The amount allotted for travel is $1,800 per year.

    For all Department of Defense-funded research involving human subjects, medical care for research-related injuries must be provided at no cost to the subject. Many institutions and states provide for this medical care as part of their liability insurance. If not, investigators should plan on budgeting for such costs. The institution business office can assist applicants with budgeting for this requirement. See Appendix F, part 7 for more details.

19. Instruments – See Appendix B, part 19.

20. Publications and/or Patent Abstracts – See Appendix B, part 20.

21. Proposal Submission – See Appendix B, part 21.

22. Submission Deadline – See Appendix B, part 22.
    Please note that one electronic PDF version of your proposal must be uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002. Submission of a proposal after the deadline may be grounds for proposal rejection.**

23. Regulatory Compliance and Quality Requirements – See Appendix B, part 23.
    The one-page Certificate of Environmental Compliance and one-page Principal Investigator Safety Program Assurance documents are to be submitted with the proposal. All documents related to Regulatory Compliance and Quality issues should be available on the CDMRP web site by April 2002. See Appendix B, part 23 for more details.

Principal Investigator: _____
Last Name *First Name* *MI*

Proposal Title: _____

_____

New Investigator Award Proposal
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STATEMENT OF ELIGIBILITY

FY02 NFRP New Investigator Award

Applicant's Name: _____

Title of Proposal: _____

Applicant's Organization Name: _____

Applicant's Organization Location: _____

_____

Signature of Applicant: _____

I certify that the above-named investigator fulfills the requirements to be considered for a New Investigator Award and specifically meets all of the following criteria:

- Is an independent (i.e., non-mentored) investigator;
- Is below the level of Associate Professor or equivalent; and
- Has access to appropriate research facilities.

Name of Official (*please print*): _____

Title: _____

Organization: _____

Signature of Official: _____ Date: _____

IV. Idea Awards

IV-A. Idea Awards

The intent of Idea Awards is to encourage innovative ideas and technology relevant to neurofibromatosis (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 may present 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. It is the responsibility of the investigator to clearly articulate how the proposed research is innovative.

Idea Award proposals are qualitatively different from traditional research proposals as outlined in Table IV-1. Although Idea Award proposals do not require preliminary data, they should be based on a sound scientific rationale established through a critical review and analysis of the literature and/or logical reasoning. Applicants for Idea Awards must have a publication record, although they do not need to have publications in the field of NF. While not required, multi-institutional and multidisciplinary research collaborations are encouraged.

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

Type of Proposal	Preliminary Data	Mechanism Purpose
Idea Award Proposal	Not required (can be included if available)	To fund novel, high-risk research that challenges existing paradigms
New Investigator Award Proposal	Not required (can be included if available)	To prepare new, independent investigators below the level of Associate Professor
Traditional Research Proposal	Required	To expand well-established avenues of research

Funding for Idea Awards can be requested for an average of $150,000 per year in direct costs for a maximum of $450,000 over 3 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. The amount allotted for travel is $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.

Submission of the same research project to the Fiscal Year 2002 (FY02) Neurofibromatosis Research Program (NFRP) under different award mechanisms is not allowed, and all such duplicate submissions may be administratively withdrawn. This includes submissions under different award mechanisms by different Principal Investigators (PIs). The Government reserves the right to reject any proposal.

IV-B. Scientific Peer Review Evaluation Criteria for Idea Award Proposals

Idea Award proposals will be evaluated according to the following criteria:

- **Innovation:** Is the proposed research innovative in one or more of the following areas: study concept or question; research methods or technologies; clinical interventions; adaptations of existing methods or technologies? Is it innovative in other ways? Are the aims original? Does the project propose new paradigms or challenge existing paradigms? Is the project one for which innovation is not necessary?

- **Research Strategy:** Are the conceptual framework, hypothesis, design, methods, and analyses adequately developed and well integrated to the aims of the project? Is a clear-cut rationale supporting the research strategy provided? 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?

- **Relevance:** Does this study address a critical problem in NF research? If the aims of the research are achieved, will the results be of benefit to the field of NF research or persons affected by the disease? Does the application 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 study? Does the PI have a publication record (not necessarily including publications in the field of NF)? Is the proposed work appropriate to the experience level of the PI? Is there representation from all the expertise areas needed to conduct the study successfully?

- **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?

- **Budget:** Is the budget appropriate for the research proposed?

IV-C. Programmatic Review Evaluation Criteria for Idea Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance. For example, does the proposal meet the goals and intent of the Idea Award mechanism? Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

IV-D. Letter of Intent

All applicants considering submission of a proposal in response to this program announcement are requested to submit an electronic Letter of Intent no later than May 21, 2002. This form is available on the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil/funding/02nfrp1

IV-E. Proposal Preparation

Instructions for proposal preparation for all award mechanisms are found in Appendix B. The following supplemental information is specific for Idea Awards. Please note that the body of the proposal is limited to **10 pages**, inclusive of any figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn by the Government prior to peer review.** Applicants are required to submit the Proposal Information prior to upload/submission of the proposal. Ensure that one electronic Portable Document Format (PDF) version of your proposal, which will serve as the official proposal submission, is uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002.**

Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

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

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

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Information – See Appendix B, part 4 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.

6. Table of Contents – See Appendix B, part 6.
   Use the table of contents found at the end of this section in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the

Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8 and Appendix D.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.

11. Proposal Body – See Appendix B, part 11.
    The body of Idea Award proposals is limited to **10 pages**, inclusive of figures, tables, graphs, and photographs, if used.

    It is the responsibility of the applicant to clearly articulate how the proposed research is innovative. The inclusion of preliminary data is **not** required; however, investigators must demonstrate a sound scientific rationale established through a critical review and analysis of the literature and/or logical reasoning.

    Describe the proposed project using the general outline provided below:

    a. Background: Briefly describe the ideas behind the proposed work and cite relevant literature references. Describe previous experience most pertinent to this proposal.

    b. Hypothesis/Rationale/Purpose: State the hypothesis to be tested, the expected results, and why the proposed study is innovative.

    c. Objectives: State concisely the specific aims and the research strategy of the study.

    d. Methods: Describe the experimental design and methodology. If the methodology is new or unusual, describe it in sufficient detail for evaluation.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14 and Appendix E.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.

17. Administrative Documentation – See Appendix B, part 17.

18. Detailed Cost Estimate – See Appendix B, part 18.
    Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. In addition, budgets will be reviewed during award negotiations. Please provide complete justification for expenses in all categories. Funding for Idea Awards can be requested for an average of $150,000 per year in direct costs for a maximum of $450,000 over 3 years, plus indirect costs as appropriate. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. The amount allotted for travel is $1,800 per year.

    For all Department of Defense-funded research involving human subjects, medical care for research-related injuries must be provided at no cost to the subject. Many institutions and states provide for this medical care as part of their liability insurance. If not, investigators should plan on budgeting for such costs. The institution business office can assist applicants with budgeting for this requirement. See Appendix F, part 7 for more details.

19. Instruments – See Appendix B, part 19.

20. Publications and/or Patent Abstracts – See Appendix B, part 20.

21. Proposal Submission – See Appendix B, part 21.

22. Submission Deadline – See Appendix B, part 22.
    Please note that one electronic PDF version of your proposal must be uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002. Submission of a proposal after the deadline may be grounds for proposal rejection.**

23. Regulatory Compliance and Quality Requirements – See Appendix B, part 23.
    The one-page Certificate of Environmental Compliance and one-page Principal Investigator Safety Program Assurance documents are to be submitted with the proposal. All documents related to Regulatory Compliance and Quality issues should be available on the CDMRP web site by April 2002. See Appendix B, part 23 for more details.

Principal Investigator: _____
Last Name *First Name* *MI*

Proposal Title: _____

_____

Idea Award Proposal
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V. Career Development Awards

V-A. Career Development Awards

Career Development Awards (CDAs) are designed to encourage established scientists or research clinicians who are currently working in areas other than neurofibromatosis (NF) to shift their focus to NF research. Such awards will provide investigators who are new to NF research the opportunity to acquire the training, data, and experience to compete for traditional awards. Clinically oriented physicians who wish to undertake clinical research in NF are encouraged to submit CDA proposals.

For the purpose of this program, a CDA is intended for an individual who has his or her own established independent program of research with limited or no experience in the NF field (as indicated by publications and research funding) and holds a position equivalent to or higher than the rank of Associate Professor.

CDA proposals should include a discussion of the level of institutional commitment to fostering the applicant's research career as reflected by (1) the extent to which the applicant will be relieved of his or her academic or clinical responsibilities to have additional time for research, and (2) opportunities for critical professional interaction with colleagues working in the field of NF. A letter of support from the institution needs to be included as part of the proposal.

Funding for CDAs can be requested for an average of $60,000 per year in direct costs for a maximum of $180,000 over 3 years, plus indirect costs as appropriate. Direct costs can cover only salary support and travel to scientific meetings. The amount allotted for travel is $1,800 per year.

V-B. Scientific Peer Review Evaluation Criteria for Career Development Award Proposals

CDA proposals will be evaluated according to the following criteria:

- **Candidate:** Do the candidate's previous training, prior research experience, and publication record indicate promising achievements to date? Is there a need for the proposed research experience and training in order for the candidate to develop into an independent NF investigator? Has the candidate demonstrated a personal commitment to pursuing a career in NF research, including an appropriate level of effort on this proposal? If appropriate, does the applicant have experience in conducting clinical trials?

- **Relevance:** Does the candidate's research program 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 application 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 decreasing the impact of NF and/or advancing research in the field?

- **Institutional Commitment:** Is there a strong institutional commitment to relieve the candidate from other academic or clinical responsibilities in order to permit substantially increased time for research activities? Is the institution prepared to provide adequate laboratory facilities, equipment, and opportunities for critical professional interaction with other colleagues in the field of NF? Is there a strong institutional commitment to the candidate's development?

- **Budget:** Is the budget appropriate?

V-C. Programmatic Review Evaluation Criteria for Career Development Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the CDA mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

V-D. Letter of Intent

All applicants considering submission of a proposal in response to this program announcement are requested to submit an electronic Letter of Intent no later than May 21, 2002. This form is available on the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil/funding/02nfrp1

V-E. Proposal Preparation

Instructions for proposal preparation for all award mechanisms are found in Appendix B of this program announcement. The following supplemental information is specific for CDAs. Please note that the body of the proposal is limited to **6 pages**, inclusive of any figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn by the Government prior to peer review.** Applicants are required to submit the Proposal Information prior to upload/submission of the proposal. Ensure that one electronic Portable Document Format (PDF) version of your proposal, which will serve as the official proposal submission, is uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002.**
Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

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

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

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Information – See Appendix B, part 4 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.

6. Table of Contents – See Appendix B, part 6.
   Use the table of contents on page V-6 in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the Principal Investigator (PI) name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8 and Appendix D.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.
    Applicants should articulate how the combination of training and relevance to NF will catalyze the applicant's development as an independent NF investigator.

11. Proposal Body – See Appendix B, part 11.
    The body of CDA proposals is limited to **6 pages**.

    a. Career Development Plans: Briefly describe the candidate's career development plan and how the proposed experience and training will promote the candidate's career development in the area of NF research. Discuss the applicant's research plans after the completion of this award.

    b. Description of Research Project: Applicants should provide an overview of how their time will be spent once relieved from other academic or clinical responsibilities.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14 and Appendix E.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.

17. Administrative Documentation – See Appendix B, part 17.
    In addition to the documentation described in Appendix B, provide the following items in the Administrative Documentation section of the proposal submission:

    - A form signed by the Department Chair, Program Director, or Dean indicating that the PI is an eligible applicant for this award type. Use the Statement of Eligibility Form on page V-7. This form must be signed and then scanned into the PDF file of your proposal prior to its submission to the CDMRP.

    - A letter of institutional support showing the level of institutional commitment to fostering the applicant's research career as reflected by (1) the extent to which the applicant will be relieved of other academic or clinical responsibilities to have additional time for research, and (2) opportunities for critical professional interaction with colleagues in the field of NF. This letter needs to be signed and then scanned into the PDF file of your proposal prior to its submission to the CDMRP.

18. Detailed Cost Estimate – See Appendix B, part 18 and Appendix F.
    Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. In addition, budgets will be reviewed during award negotiations. Please provide complete justification for expenses in all categories. Funding for CDAs can be requested for an average of $60,000 per year in direct costs for a maximum of $180,000 over 3 years, plus indirect costs as appropriate. Direct costs can cover only salary support and travel to scientific meetings. Funds for research must be provided from another resource and should be noted in the Existing/Pending Support section. The amount allotted for travel is $1,800 per year to attend scientific meetings.

    For all Department of Defense-funded research involving human subjects, medical care for research-related injuries must be provided at no cost to the subject. Many institutions and states provide for this medical care as part of their liability insurance. If not, investigators should plan on budgeting for such costs. The institution business office can assist applicants with budgeting for this requirement. See Appendix F, part 7 for more details.

19. Instruments – See Appendix B, part 19.

20. Publications and/or Patent Abstracts – See Appendix B, part 20.
21. Proposal Submission – See Appendix B, part 21.

22. Submission Deadline – See Appendix B, part 22.
    Please note that one electronic PDF version of your proposal must be uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time)**

June 4, 2002. Submission of a proposal after the deadline may be grounds for proposal rejection.

23. Regulatory Compliance and Quality Requirements – See Appendix B, part 23.
The one-page Certificate of Environmental Compliance and one-page Principal Investigator Safety Program Assurance documents are to be submitted with the proposal. All documents related to Regulatory Compliance and Quality issues should be available on the CDMRP web site by April 2002. See Appendix B, part 23 for more details.

Principal Investigator: _____
Last Name *First Name* *MI*

Proposal Title: _____

_____

Career Development Award Proposal
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STATEMENT OF ELIGIBILITY

FY02 NFRP Career Development Award

Applicant's Name: _____

Title of Proposal: _____

Applicant's Organization Name: _____

Applicant's Organization Location: _____

_____

Signature of Applicant: _____

I certify that the above-named investigator fulfills the requirements to be considered for a Career Development Award and specifically meets the following sets of criteria:

- Has his or her own established independent program of research with limited or no experience in the field of neurofibromatosis, and
- Holds a position as an Associate Professor or equivalent or above

Name of Official (*please print*): _____

Title: _____

Organization: _____

Signature of Official: _____ Date: _____

VI. Investigator-Initiated Research Awards (with optional Nested Postdoctoral Traineeship[s])

VI-A. Investigator-Initiated Research Awards

The intent of Investigator-Initiated Research Awards (IIRAs) is to sponsor basic and clinically oriented research that will (1) provide insight into the molecular mechanisms underlying the development of neurofibromatosis (NF), (2) result in substantial improvement(s) over today's approach to the diagnosis and treatment of either NF1 or NF2, and (3) enhance the quality of life for persons with the disease. These grants are intended to fund independent investigators across a broad spectrum of disciplines. An IIRA investigator is defined as an independent investigator at a level equivalent to or above that of Assistant Professor. All IIRA proposals must include preliminary data relevant to NF research and the proposed project. **In addition, the proposal should include a clear statistical plan of analysis.**

The Fiscal Year 2002 (FY02) NFRP encourages investigators to submit IIRA proposals that:

- Perform cellular and biochemical studies investigating the normal functioning of the NF1 and NF2 proteins and how abnormal functioning and mutagenesis of the NF1 and NF2 genes lead to pathogenesis;
- Expand the knowledge of the genes that contribute to NF beyond the GAP[1]-related domain in NF1;
- Attempt to define the genetic and nongenetic factors and modifiers that play a role in the manifestations of NF1 and NF2, 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 methods of imaging and measurement of lesions;
- Develop new approaches to the quantification of dermal neurofibromas;
- Study the pathogenesis of pseudoarthrosis, scoliosis, and other bone abnormalities in NF1; and
- Address early childhood developmental and psychosocial aspects (e.g., learning disabilities and other cognitive aspects) of NF1.

[1] GTPase-activating protein

Although there are no total dollar amount restrictions to these awards, funding for IIRAs can only be requested for up to 4 years. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. The amount allotted for travel is $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. While not required, multi-institutional and multidisciplinary research collaborations are encouraged.

Submission of the same research project to the FY02 Neurofibromatosis Research Program (NFRP) under different award mechanisms will not be allowed, and all such duplicate submissions may be administratively withdrawn. This includes submissions under different award mechanisms by different Principal Investigators (PIs). The Government reserves the right to reject any proposal.

VI-B. IIRAs with Nested Postdoctoral Traineeship(s)

Nested Postdoctoral Traineeships are being offered as an optional part of IIRA 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 IIRA proposal. However, these Nested Postdoctoral Traineeships can only be obtained as an optional part of the IIRA mechanism. Applicants must submit a biographical sketch of no more than three pages for each trainee and include it in the biographical sketch section (see Appendix B, part 14). "To be named" trainees are acceptable for the proposal submission. For proposals approved for funding, the U.S. Army Medical Research Acquisition Activity must be provided with the name and biographical sketch of each applicant for review and approval.

For the Nested Postdoctoral Traineeship portion of IIRA proposals, funding can be requested for a maximum of $60,000 per year inclusive of direct and indirect costs for a maximum of $240,000 per trainee over 4 years. 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 (see Appendix B, part 18).

VI-C. Scientific Peer Review Evaluation Criteria for IIRA Proposals

IIRA 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 there 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 research support the proposed project? Is the experimental design sound and sufficiently well developed with the required statistical power to lead to significant results?

- **Relevance:** To what extent will the project, if successful, make an original and important contribution to the goal of advancing research in the field? 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 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 field? Is the proposed work appropriate to the experience level of the PI and other researchers (if any)? Is appropriate expertise available to conduct the study successfully? **For IIRAs with Nested Postdoctoral Traineeship(s)**, are the PI and other scientific personnel well qualified to conduct training for the trainee(s)? Is there a senior staff member who is identified and responsible for the trainee(s)? Is the trainee at an appropriate stage in his or her career for such training and has the trainee made a commitment to enter the field of NF?

- **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 IIRAs 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 being studied?

- **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?

VI-D. Programmatic Review Evaluation Criteria for IIRA Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the IIRA mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

VI-E. Letter of Intent

All applicants considering submission of a proposal in response to this program announcement are requested to submit an electronic Letter of Intent no later than May 21, 2002. This form is available on the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil/funding/02nfrp1

VI-F. Proposal Preparation

Instructions for proposal preparation for all award mechanisms are found in Appendix B of this program announcement. The following supplemental information is specific for IIRAs. Please note that the body of the proposal is limited to **20 pages**, inclusive of figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn by the Government prior to peer review.** Applicants are required to submit the Proposal Information prior to upload/submission of the proposal. Ensure that one electronic Portable Document Format (PDF) version of your proposal, which will serve as the official proposal submission, is uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002.**

Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

1. Who May Apply – See Appendix B, part 1.
   Eligible applicants for Nested Postdoctoral Traineeships are postdoctoral students with 3 years or less of experience at the time of proposal submission. At the time of award negotiations, an applicant must have successfully defended a doctoral thesis and completed all academic requirements.

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

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Information – See Appendix B, part 4 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.

6. Table of Contents – See Appendix B – Part 6.
   Use the table of contents at the end of this section in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8 and Appendix D.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.

11. Proposal Body – See Appendix B, part 11.

    a. IIRA Proposal Body.
    The body of IIRA proposals is limited to **20 pages**, inclusive of figures, tables, graphs, and photographs, if used.

    The inclusion of preliminary data **is required** for IIRA proposals; investigators must submit promising and well-founded preliminary data relevant to NF and the proposed project.

    Describe the proposed project using the general outline provided below:

    i. Background: Describe the ideas behind the proposed work and cite relevant literature references. Describe previous experience most pertinent to this proposal.

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

    iii. Objectives: State the specific aims and the research strategy of the study.

    iv. Preliminary Data: Provide pertinent data to support the necessity, feasibility, and potentiality of the proposed project.

    v. Methods: Describe the experimental design and methodology.

    b. Nested Postdoctoral Traineeship Proposal Body.
    The body of the Nested Postdoctoral Traineeship proposal is limited to **2 pages**. Identify the staff members who are responsible for the trainees. Describe the research training in which the trainees will participate such as research, coursework, laboratory techniques, conferences, and journal clubs.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.

17. Administrative Documentation – See Appendix B, part 17.

18. Detailed Cost Estimate – See Appendix B, part 18.
    Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. In addition, budgets will be reviewed during award negotiations. Please provide complete justification for expenses in all categories. There are no total dollar amount restrictions for IIRA proposals but funding can only be requested for up to 4 years. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. Funding for Nested Postdoctoral Traineeships can be requested for a maximum of $60,000 per year inclusive of direct and indirect costs for a maximum of $240,000 per trainee over 4 years. Direct costs can cover salary, stipends, seminars and courses, expenses including research supplies, equipment, and travel to scientific meetings. The amount allotted for travel is $1,800 per year for the PI. The amount allotted for postdoctoral trainee travel is $1,500 per year.

    For all Department of Defense-funded research involving human subjects, medical care for research-related injuries must be provided at no cost to the subject. Many institutions and states provide for this medical care as part of their liability insurance. If not, investigators should plan on budgeting for such costs. The institution business office can assist applicants with budgeting for this requirement. See Appendix F, part 7 for more details.

19. Instruments – See Appendix B, part 19.

20. Publications and/or Patent Abstracts – See Appendix B, part 20.

21. Proposal Submission – See Appendix B, part 21.

22. Submission Deadline – See Appendix B, part 22.
    Please note that one electronic PDF version of your proposal must be uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002. Submission of a proposal after the deadline may be grounds for proposal rejection.**

23. Regulatory Compliance and Quality Requirements – See Appendix B, part 23.
    The one-page Certificate of Environmental Compliance and one-page Principal Investigator Safety Program Assurance documents are to be submitted with the proposal. All documents related to Regulatory Compliance and Quality issues should be available on the CDMRP web site by April 2002. See Appendix B, part 23 for more details.

Principal Investigator: _____
Last Name *First Name* *MI*

Proposal Title: _____

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Investigator-Initiated Research Award Proposal
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VII. Therapeutic Development Awards

VII-A. Therapeutic Development Awards

In an effort to boost the number of clinical trials within the neurofibromatosis (NF) research field, the Neurofibromatosis Research Program (NFRP) is offering the Therapeutic Development Award. The intent of this award mechanism is to sponsor the development and evaluation of preclinical model systems for NF1 and NF2. More specifically, this award supports research projects in one or more of the following phases of the preclinical drug development process:

- Development of new or modification of existing in vitro or in vivo preclinical model systems for elucidating the actions of potential drugs for NF. Preclinical model systems can include cell-based assays, mammalian or non-mammalian models, or high-throughput assays.
- Confirmation of the predictive value of newly developed or existing in vitro or in vivo preclinical model systems.
- Use of established model systems to screen and/or determine the therapeutic potential of drugs for NF.

The overall goal of this award mechanism is to allow NF investigators to develop the skills and generate the preclinical data necessary to conduct clinical trials after completion of the research. The Therapeutic Development Award is not restricted to research in malignant neoplasias, but is open to the full spectra of manifestations of NF1 and NF2. The proposed studies are expected to be empirical in nature and product-driven rather than hypothesis-driven. It is anticipated that the agents and model systems generated from these awards will lead to the development of a broad platform on which to test future therapies.

Specific programmatic interests include proposals that:

- Develop model systems to test potential lead agents or therapies for NF;
- Develop high-throughput models to aid in defining targets;
- Make existing preclinical model systems for NF suitable for pharmacological screening;
- Improve the understanding of mechanism of action of new therapies;
- Evaluate the molecular mechanisms underlying the actions of pharmacological agents;
- Test new therapies for NF using established preclinical model systems; or
- Link biological, molecular, and biochemical effects in the experimental design.

The preclinical drug development process may require resources beyond those available at a single institution. Therefore, Therapeutic Development Awards are open to investigators interested in establishing synergistic, goal-focused, multi-institutional consortia (e.g., between industry and academia or between multiple academic institutions) focused on developing and validating animal models for their use in preclinical testing, identifying lead agents, and testing the clinical potential of the lead agents developed by the investigators. The formation of consortia between biochemists and molecular biologists focused on target validation and evaluation is encouraged. If a consortium is proposed, sufficient characterization of the consortium and justification for the collaborative partners must be included in the proposal (see Section VII-B).

Although there are no total dollar amount restrictions to these awards, programmatic priority will be given to smaller-scale, cost-efficient projects with well-defined endpoints. Funding can be requested for up to 3 years. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. The amount allotted for travel is $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. For proposals involving a consortium, direct costs can also cover expenses for meetings that bring together members of the consortium.

All applicants for Therapeutic Development Awards **must include preliminary data** relevant to the phase(s) of the preclinical drug development process covered by the research in their proposals. Applicants should provide a clear scientific rationale for bringing agents from the laboratory to the clinic. In addition, studies should have clear pharmacological endpoints. If appropriate, the proposal should include a clear statistical plan of analysis. The Fiscal Year 2002 (FY02) NFRP encourages applicants from non-academic institutions (e.g., biotech) to apply to this award mechanism. Priority will be given to proposals that meet the specific goal of the program (i.e., developing therapeutic agents for NF).

Submission of the same research project to the FY02 NFRP under different award mechanisms is not allowed, and all such duplicate submissions may be administratively withdrawn. This includes submissions under different award mechanisms by different Principal Investigators (PIs). The Government reserves the right to reject any proposal.

VII-B. Scientific Peer Review Evaluation Criteria for Therapeutic Development Award Proposals

Therapeutic Development Award proposals will be evaluated according to the following criteria:

- **Research Strategy:** Does the applicant provide preliminary data that support the approach and scientific rationale for the study? Are the conceptual framework, design, methods, and analyses adequately developed and well integrated to support the feasibility and promise of the approach? Is the experimental design sound and sufficiently well developed with the required statistical method and analysis plan to lead to significant results? Is the appropriate statistical expertise represented on the research team? Does the applicant acknowledge

potential problem areas and consider alternative methods/tactics?

- **Therapeutic Relevance:** Does the applicant make a convincing case for the relevance of the preclinical model to the development of NF therapeutics? Is evidence provided for the predictive value of the preclinical model? Is there a clear scientific rationale for bringing agents from the laboratory to the clinic? Does the study have clear pharmacological endpoints? If lead agents are being screened, how relevant are they to NF? How does this research advance the agenda of bringing therapies to clinical trials?

- **Principal Investigator and Personnel:** Is the PI appropriately trained and well suited to carry out this work? Are the other scientific personnel well qualified to participate in the project? Is there appropriate representation from all areas of expertise needed to conduct the study successfully? If a consortium is proposed, is the team appropriate for addressing the proposed project?

- **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 proposals involving consortia:** Is there evidence that the consortium is goal-focused? Is there adequate synergy between the involved institutions/organizations? Is there a clear plan for interaction between members of the consortium? Do the institutions/ organizations involved in the project strengthen the proposal?

- **Budget:** Is the budget appropriate for the research proposed?

VII-C. Programmatic Review Evaluation Criteria for Therapeutic Development Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the Therapeutic Development Award mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

VII-D. Letter of Intent

All applicants considering submission of a proposal in response to this program announcement are requested to submit an electronic Letter of Intent no later than May 21, 2002. This form is available on the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil/funding/02nfrp1

VII-E. Proposal Preparation

Instructions for proposal preparation for all award mechanisms are found in Appendix B. The following supplemental information is specific for Therapeutic Development Awards. Please note that the body of the proposal is limited to **20 pages**, inclusive of figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn by the Government prior to peer review.** Applicants are required to submit the Proposal Information prior to upload/submission of the proposal. Ensure that one electronic Portable Document Format (PDF) version of your proposal, which will serve as the official proposal submission, is uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002.**

Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

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

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

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Information – See Appendix B, part 3 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.

6. Table of Contents – See Appendix B, part 6.
   Use the table of contents found at the end of this section in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8 and Appendix D.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.

11. Proposal Body – See Appendix B, part 11.
    The body of Therapeutic Development Award proposals is limited to **20 pages**, inclusive of figures, tables, graphs, and photographs, if used. The inclusion of preliminary data **is required** for all Therapeutic Development Award proposal submissions. Investigators must submit promising and well-founded preliminary data relevant to NF and the proposed project.

    Describe the proposed project using the general outline below:

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

    b. Rationale: State the purpose of the study and the expected results.

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

    d. Preliminary Data: Provide pertinent data to support the necessity, feasibility, and potentiality of the proposed project.

    e. Methodology: Describe the experimental design and methodology, including statistical analysis.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.
    Clinical, data management, and laboratory facilities, as well as required equipment should be described in detail for **all** participating institutions.

17. Administrative Documentation – See Appendix B, part 17.

18. Detailed Cost Estimate – See Appendix B, part 18.
    Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. In addition, budgets will be reviewed during award negotiations. Please provide complete justification for expenses in all categories. There are no total dollar amount restrictions for Therapeutic Development Award proposals, but funding can only be requested for 3 years. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. A budget for the entire period of the grant must be provided. 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. For proposals involving a consortium, direct costs can also cover expenses for meetings that bring together members of the consortium. The amount allotted for travel is $1,800 per year.

For all Department of Defense-funded research involving human subjects, medical care for research-related injuries must be provided at no cost to the subject. Many institutions and states provide for this medical care as part of their liability insurance. If not, investigators should plan on budgeting for such costs. The institution business office can assist applicants with budgeting for this requirement. See Appendix F, part 7 for more details.

19. Instruments – See Appendix B, part 19.

20. Publications and/or Patent Abstracts – See Appendix B, part 20.

21. Proposal Submission – See Appendix B, part 21.

22. Submission Deadline – See Appendix B, part 22.
    Please note that one electronic PDF version of your proposal must be uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002. Submission of a proposal after the deadline may be grounds for proposal rejection.**

23. Regulatory Compliance and Quality – See Appendix B, part 23.
    The one-page Certificate of Environmental Compliance and one-page Principal Investigator Safety Program Assurance documents are to be submitted with the proposal. All documents related to Regulatory Compliance and Quality issues should be available on the CDMRP web site by April 2002. See Appendix B, part 23 for more details.

Principal Investigator: _____
Last Name *First Name* *MI*

Proposal Title: _____

_____

Therapeutic Development Award Proposal
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VIII. Clinical Trial Awards

VIII-A. Clinical Trial Awards

The intent of Clinical Trial Awards is to sponsor patient-oriented research with the potential to have a major impact on the treatment of either neurofibromatosis 1 (NF1) or NF2. Clinical Trial Awards will support Phase 1 and Phase 2 clinical trials; separate discussions are provided below for each type of clinical trial. Applicants should clearly specify in their proposals for which type of Clinical Trial Award they are applying. The ultimate goal of the Clinical Trial Award mechanism is to sponsor novel clinical research that has the potential to substantially improve today's approach to the treatment of NF1 and NF2.

Phase 1 clinical trials should focus on determining the safety, toxicity, tolerability, and pharmacokinetics of new agents or treatment schedules. It is expected that this award will allow the recipient the opportunity to obtain the data and experience necessary to conduct a Phase 2 clinical trial. Applicants for Phase 1 trials must include a clear scientific rationale for the trial as well as adequate preclinical supplemental data to support the feasibility of their hypotheses and approaches. Applicants must include a detailed plan for completing the Phase 1 trial during the course of the award and a clear experimental and appropriately powered statistical plan to perform the clinical trial. Phase 1 applicants are encouraged to pursue correlative studies.

Phase 2 clinical trials should focus on defining the efficacy of new agents. Applicants for Phase 2 clinical trials must include Phase 1 or Pilot clinical trial data and adequate preclinical supplemental data to support the feasibility of their hypotheses and approaches, along with a detailed plan to complete the Phase 2 clinical trial during the course of the award. Applicants must also include a clear experimental and appropriately powered statistical plan to perform the Phase 2 clinical trial. Applicants are encouraged to submit studies that further test the safety of a novel combination of agents before it is used on a larger number of patients in a Phase 3 clinical trial.

The Clinical Trial Award is not limited to therapeutic studies. Applicants are encouraged to submit proposals focusing on (1) identifying targets, (2) developing endpoints and tools for measuring outcomes, or (3) developing drugs. However, as noted above, a clinical trial must be conducted as part of the study.

Although there are no total dollar amount restrictions to these awards, programmatic priority will be given to smaller scale, cost-efficient clinical trials. The Neurofibromatosis Research Program (NFRP) is particularly interested in proposals for Phase 1 clinical trials that are under $500,000. Funding for Phase 1 clinical trials can be requested for up to 3 years, while funding for Phase 2 clinical trials can be requested for up to 4 years. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. 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. Consideration of cost-sharing with other funding sources and multi-institutional/multidisciplinary research collaborations are encouraged.

Applicants are encouraged to use the existing infrastructures of the NFRP-funded NF1 and NF2 natural history studies as infrastructures for their proposed clinical trials.

Submission of the same research project to the Fiscal Year 2002 NFRP under different award mechanisms is not allowed, and all such duplicate submissions may be administratively withdrawn. This includes submissions under different award mechanisms by different Principal Investigators (PIs). The Government reserves the right to reject any proposal.

VIII-B. Scientific Peer Review Evaluation Criteria for Clinical Trial Award Proposals

Clinical Trial Award 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? Does the applicant provide a clear scientific rationale for the trial? Have the logistical aspects of the proposed clinical trial been appropriately addressed? Has the availability of subjects for the clinical trial, the prospect of their participation, and the likelihood of subject attrition been addressed? Is the recruitment schedule reasonable?

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

- **Statistical Plan:** For the proposed clinical trial, 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?

- **Principal Investigator and Personnel:** Does the PI have expertise in NF? Is the PI appropriately trained and well suited to carry out this work? 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:** Is there evidence for an appropriate clinical setting and the availability of institutional resources to support the study at each participating center? Are there assurances that therapies to be used are available? Are letters of commitment included from participating centers?

- **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?

VIII-C. Programmatic Review Evaluation Criteria for Clinical Trial Award Proposals

Funding recommendations at this second tier of review are based on a comparative process. Applicants are reminded of the importance of programmatic relevance and the importance of meeting the intent of the Clinical Trial Award mechanism. Additional details on programmatic review procedures and evaluation criteria are included in Section I-C.

VIII-D. Letter of Intent

All applicants considering submission of a proposal in response to this program announcement are requested to submit an electronic Letter of Intent no later than May 21, 2002. This form is available on the Congressionally Directed Medical Research Programs (CDMRP) web site at http://cdmrp.army.mil/funding/02nfrp1

VIII-E. Proposal Preparation

Instructions for proposal preparation for all award mechanisms are found in Appendix B. The following supplemental information is specific for Clinical Trial Awards. Please note that the body of the proposal is limited to **50 pages**, inclusive of figures, tables, graphs, and photographs. **Proposals exceeding specified page limits may be administratively withdrawn by the Government prior to peer review.** Applicants are required to submit the Proposal Information prior to upload/submission of the proposal. Ensure that one electronic Portable Document Format (PDF) version of your proposal, which will serve as the official proposal submission, is uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002.**

Applicants unfamiliar with the preparation of PDF files are encouraged to acquire the software and learn the process before the submission deadline.

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

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

3. Resubmissions and Duplicate Submissions – See Appendix B, part 3.

4. Proposal Information – See Appendix B, part 4 and Appendix C.

5. Title/Referral Page – See Appendix B, part 5.
   In the Award Mechanism section of the Title/Referral Page, indicate whether the proposal is for a Phase 1 or Phase 2 clinical trial.

6. Table of Contents – See Appendix B, part 6.
   Use the table of contents found at the end of this section in your proposal submission. This table of contents should be used as a guide for assembling all required components of the proposal. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission – See Appendix B, part 7.

8. Proposal Abstracts – See Appendix B, part 8 and Appendix D.

9. Statement of Work – See Appendix B, part 9 and Appendix D.

10. Proposal Relevance Statement – See Appendix B, part 10.

11. Proposal Body – See Appendix B, part 11.
    The body of Clinical Trial Award proposals is limited to **50 pages**.
    Phase 1 and Phase 2 clinical trial applicants must submit promising and well-founded preliminary data relevant to NF and the proposed project. In addition, the inclusion of Phase 1 or Pilot clinical trial data is required for Phase 2 clinical trial applicants.

    Describe the proposed project using the general outline below:

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

    b. Rationale: State the purpose of the study and the expected results.

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

    d. Preliminary Studies: A presentation of the studies that led to the proposed clinical trial is required. In addition, Phase 2 clinical trial applicants must provide Phase 1 or Pilot clinical trial data.

    e. Clinical Protocol: Include a discussion of the following topics.

        i. Study design for the intervention(s) to be used.

        ii. Potential biases in the research protocol and how they will be addressed.

        iii. Clinical, behavioral, laboratory, and physiological tests and protocols.

        iv. Patient recruitment, including (1) patient availability; (2) inclusion and exclusion criteria; (3) methods for recruiting, retention, and follow-up; (4) data to support recruitment/retention estimates; (5) patient assignment to experimental groups and methods of randomization (if any); and (6) study endpoints.

v. Data management, including the (1) overall approach to data management; (2) a statistical plan that includes sample size calculations and methods to monitor quality and consistency of both the intervention(s) and data collection; and (3) data security measures.

vi. Methods of analysis (primary and secondary endpoints should be clearly defined and related to the power calculation).

vii. Any issues that may lead to concern for the welfare of human subjects and confidentiality.

viii. A study organization and management plan, including an organizational chart and timetable.

12. Abbreviations – See Appendix B, part 12.

13. References – See Appendix B, part 13.

14. Biographical Sketches – See Appendix B, part 14.

15. Existing/Pending Support – See Appendix B, part 15.

16. Facilities/Equipment Description – See Appendix B, part 16.
    Clinical, data management, and laboratory facilities, as well as required equipment should be described in detail for **all** participating institutions.

17. Administrative Documentation – See Appendix B, part 17.

18. Detailed Cost Estimate – See Appendix B, part 18.
    Budget is a consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. In addition, budgets will be reviewed during award negotiations. Please provide complete justification for expenses in all categories. There are no total dollar amount restrictions for Clinical Trial Award proposals but funding can only be requested for 3 years for Phase 1 clinical trials and 4 years for Phase 2 clinical trials. Direct costs can cover salary, expenses including research supplies, costs for research-related injury medical costs (if applicable; see Appendix F, part 7), and travel to scientific meetings. 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. The amount allotted for travel is $1,800 per year.

For all Department of Defense-funded research involving human subjects, medical care for research-related injuries must be provided at no cost to the subject. Many institutions and states provide for this medical care as part of their liability insurance. If not, investigators should plan on budgeting for such costs. The institution business office can assist applicants with budgeting for this requirement. See Appendix F, part 7 for more details.

19. Instruments – See Appendix B, part 29.
    Please note that for Clinical Trial Award submissions, the clinical protocol must be included in the body of the proposal and not under the Instruments section.

20. Publications and/or Patent Abstracts – See Appendix B, part 20.

21. Proposal Submission – See Appendix B, part 21.

22. Submission Deadline – See Appendix B, part 22.
    Please note that one electronic PDF version of your proposal must be uploaded/submitted by an authorized Administrative Representative of your organization's Sponsored Programs Office (or equivalent) through the Internet no later than **11:59 p.m. (applicant's local time) June 4, 2002. Submission of a proposal after the deadline may be grounds for proposal rejection.**

23. Regulatory Compliance and Quality – See Appendix B, part 23.
    The one-page Certificate of Environmental Compliance and one-page Principal Investigator Safety Program Assurance documents are to be submitted with the proposal. All documents related to Regulatory Compliance and Quality issues should be available on the CDMRP web site by April 2002. See Appendix B, part 23 for more details.

Principal Investigator: _____
Last Name *First Name* *MI*

Proposal Title: _____

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Page Number
