Appendix A

Letter of Intent

Please fill out one form for <u>each</u> proposal you intend to submit in response to the Fiscal Year 2000 Department of Defense Neurofibromatosis Research Program Announcement. Please fax, e-mail, or mail the "Letter of Intent" form to:

Fax: **301-682-5521**
E-mail: **cdmrp.pa@det.amedd.army.mil**
Mail: **Commander, U.S. Army Medical Research and Materiel Command**
ATTN: **MCMR-PLF (NFRP00-Program Announcement)**
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

You may complete and submit this form via the Congressionally Directed Medical Research Programs web site at http://cdmrp.army.mil/?/announce/forms.

Principal Investigator's Name:_____
Principal Investigator's Address:_____
_____

Phone Number:_____ **Fax Number:**_____

Intended award category to which the proposal will be submitted (please check one ONLY):

- ☐ Idea Award
- ☐ New Investigator Award
- ☐ Investigator-Initiated Research Award without Nested Postdoctoral Traineeship Award
- ☐ Investigator-Initiated Research Award with Nested Postdoctoral Traineeship Award
- ☐ Clinical Trial Award

Content area that will be addressed in the proposal (Check no more than five):

- ☐ Alternative Medicine
- ☐ Behavioral/Social Sciences
- ☐ Biological Response Modifiers
- ☐ Cell Biology
- ☐ Clinical/Experimental Therapeutics
- ☐ Clinical Genetics
- ☐ Endocrinology
- ☐ Epidemiology/Biostatistics
- ☐ Gene Expression
- ☐ Gene Sequencing/Gene Mapping
- ☐ Health Care Delivery
- ☐ Immunologic Sciences
- ☐ Molecular Genetics
- ☐ Neuroscience
- ☐ Nutrition
- ☐ Pathobiology
- ☐ Pharmacology/Toxicology
- ☐ Other, please specify _____
- ☐ Physiology
- ☐ Prevention
- ☐ Protein-Nucleic Acid Interactions
- ☐ Radiologic Sciences
- ☐ Surgery
- ☐ Technology Development
- ☐ Tumor Biology/Progression
- ☐ Virology

Proposal title and brief description:_____
_____
_____

Use an additional page if needed. Please include the name of the principal investigator and applicant institution for tracking purposes.

Please send me the following:

- ☐ Copies of the Proposal Cover Booklet - How many? _____

Appendix B

Proposal Preparation

Table of Contents

Proposal Preparation

1. Who May Apply

Eligible institutions include for-profit and nonprofit organizations, public and private, such as universities, colleges, hospitals, laboratories, companies, and agencies of local, state, and federal governments. All individuals, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by an eligible institution. The U.S. Army Medical Research and Materiel Command (USAMRMC) is especially interested in receiving applications from Historically Black Colleges and Universities/Minority Institutions (HBCU/MI).

Investigators are cautioned that awards are made to institutions. Should the principal investigator (PI) of a funded project leave the recipient institution, both the PI and an official of the recipient institution should contact the U.S. Army Medical Research Acquisition Activity (USAMRAA) awarding office prior to the PI leaving the recipient institution to discuss options available for continued support of the research project.

Set-Aside Funds for Historically Black Colleges and Other Minority Institutions

A goal of the Department of Defense (DOD) is to allocate funds for the Congressionally Directed Medical Research Programs' (CDMRP's) peer-reviewed research to fund proposals from HBCU/MI. This set-aside provision is based upon guidance from Executive Orders[1] and is intended to "advance the development of human potential, provide quality education, increase opportunities to participate in and benefit from Federal Programs and strengthen the capacity of targeted institutions." An institution's minority status is established by the Department of Education (DOEd). Proposals submitted to the DOD are assigned HBCU/MI status if they are so designated by the DOEd on the date that the Program Announcement is released. An updated DOEd list is posted on the CDMRP web site at http://cdmrp.army.mil/?/announce/minority. Any individual, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by or affiliated with an eligible institution.

HBCU/MI proposals will be reviewed concurrently with all others in the same research area during scientific peer review but may be evaluated separately during programmatic review when award recommendations are determined. Consistent with the CDMRP's goal, the final investment strategy for HBCU/MI set-aside funds will be based upon scientific excellence and program relevance.

2. Proposal Acceptance Criteria

Compliance guidelines have been designed to present the proposal in an organized and easy-to-follow manner to scientific reviewers responsible for reviewing its merit. Scientific merit reviewers will expect to see a consistent, prescribed format for each reviewed proposal. Nonadherence to format requirements (such as font size, margins, line spacing, proposal

[1] Executive Orders 12876, 12900, and 13021.

components out of order) makes proposals difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in proposal rejection or a poorer priority score in peer review. In particular, the review of applications containing more than the allotted number of pages will be restricted to the pages within the page limitations. **Excess pages may result in administrative rejection prior to peer review.**

It is required that the instructions in this section be followed carefully. The proposal must be clear and legible and conform to the following format, spacing, font size, margin, and printing guidelines:

- Spell out all acronyms the first time they are used. One page following the proposal body is allocated to spell out acronyms, abbreviations, and symbols.

- Language: English.

- Margins: Minimum of 0.5 inch top, bottom, right, and left.

- Paper Size: 8.5 x 11.0 inches. (Note to international applicants: A4 paper will be accepted if the text of the proposal does not exceed 7.5 x 10.0 inches [approximately 19 cm x 25.5 cm].)

- Printing: Single-sided. (Double-sided pages are not accepted, with the exception of article reprints.)

- Spacing: Single-spaced between lines of text, no more than five lines of type within a vertical inch.

- Type Color: Black ink including all graphs, diagrams, tables, and charts. The proposal should contain only material that can be photocopied. Submitting investigators should be cautioned that color graphs or photographs may not reproduce in subsequent photocopies. Therefore, submission of color figures, tables, graphs, or photographs is not recommended.

- Type Density: No more than 15 characters per inch. (For proportional spacing, the average for any representative section of text should not exceed either 15 characters per inch or 114 characters per line.)

- Type Font: 12 point, 10 pitch.

To assist applicants, the following example is included.

This illustrates the minimum font size and margins and the required line spacing. This illustrates the minimum font size and margins and the required line spacing. This illustrates the minimum font size and margins and the required line spacing. This illustrates the minimum font size and margins and the required line spacing. This illustrates the minimum font size and margins and the required line spacing.

3. Proposal Cover Booklet (Bubble Sheet)

Complete this form as described in Appendix C, Proposal Cover Booklet Instructions.

1. Each proposal should include one original plus three photocopies of the Proposal Cover Booklet.

2. Proposal Cover Booklets can be requested via phone, fax, e-mail, or mail at the addresses/ numbers listed in the Foreword. Please allow sufficient time for delivery by regular mail.

4. Peer Review Referral Page – Start section on a new page – No page limit

The Peer Review Referral Page must contain the following sections:

1. Proposal Title.

2. PI's Full Name, including middle initial.

3. Keyword Descriptive Technical Terms. Every effort is made to assign proposals to an appropriate peer review panel. To assist in this effort, please specify the subject area of the proposed research. Then, list specific keywords and descriptive technical terms that would best describe the technical aspects of the project (e.g., cell signaling, apoptosis, angiogenesis, drug delivery systems, gene therapy, x-ray crystallography, genetic counseling, quality of life, nuclear medicine, immunology, clinical oncology, nutrition).

4. Conflicts of Interest. Every effort is made to avoid real and apparent conflicts of interest during the peer review process. In order to assist the staff in this regard, list the names of all scientific participants in the proposal including the PI, co-investigators, research associates, research assistants, consultants, collaborators, and subcontractors. Provide the following information for each participant: name, degree(s), scientific discipline or medical specialty (e.g., radiology, immunology, clinical oncology, nutrition, pathology, cell biology, endocrinology), institutional affiliation(s), title(s), and role(s) on proposed project.

5. Proposal Title Page – Start section on a new page – 1-page limit

The Proposal Title Page should include the following information:

1. Proposal Title

2. Award Mechanism

3. PI's full name, including middle initial

4. PI's phone number, fax number, and e-mail address

5. Organization name and location (including city, state, zip or postal code, and country)

6. Name of administrative representative authorized to conduct negotiations

7. Phone number, fax number, and e-mail address of administrative representative authorized to conduct negotiations

Note: The proposed start date will be determined during contract negotiations.

6. Table of Contents – Start section on a new page – 1-page limit

Prepare a Table of Contents, with page numbers, using the outline provided in the Proposal Preparation section under each award mechanism. Number all pages of the sections consecutively at the bottom center, beginning with the Proposal Title Page.

7. Checklist for Proposal Submission Instructions

A Checklist for Proposal Submission must be completed and submitted with the proposal. Insert it immediately after the Table of Contents.

8. Proposal Abstracts – Start each abstract on a new page – 1 page each

Both a 1-page structured, technical abstract and a 1-page public (nontechnical) abstract are required. Each proposal abstract page should contain the title of the proposal and the name of the PI. **Do not include figures in either abstract.**

The abstracts are vitally important to the review of the proposal. **Programmatic review is based upon the Integration Panel's review of these two abstracts as part of the peer review summary statements; therefore, it is paramount that the investigator submit abstracts that fully describe the proposed work.**

The structured, technical abstract should provide a clear and concise overview of the proposed work, including the background, the objective or hypothesis and its supporting rationale, the significance of the proposed work to the program's goals, the specific aims of the study, and the study design.

Please use the outline below for preparing the structured, technical abstract.

1. **Background** – Provide a brief statement of the ideas and reasoning behind the proposed work.

2. **Objective/hypothesis** – State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.

3. **Specific Aims** – State concisely the specific aims of the study.

4. **Study Design** – Briefly describe the study design.

5. **Relevance** – Provide a brief statement explaining the potential relevance of the proposed work to the program's goals. For example, how the study will prevent or improve the detection or treatment of the disease.

The public abstract is intended to communicate the purpose of and rationale for the study to the nonscientific community. It should be composed in a way to make the scientific objectives of and rationale for the proposal understandable to nonscientifically-trained readers.

In addition to the abstract pages contained within the proposal, submit two additional copies of each abstract in a manila clasp envelope, along with a 3½" computer disk containing the abstract files (clearly labeled with the name of the PI, institution, and word processing program). Submit abstracts in Word, WordPerfect, or ASCII format.

Abstracts of all funded proposals will be reproduced in an abstract book and posted on the CDMRP web site at http://cdmrp.army.mil. Thus, proprietary information should not be included in the abstract.

9. Statement of Work – Start section on a new page – 2-page limit

The Statement of Work is a concise restatement of the research proposal that outlines and establishes the PI performance expectations and timeline for which the USAMRMC will provide financial support. Although some allowance is made for problems encountered and uncertainties that are a part of research, the PI is expected to meet the provisions and milestones of the Statement of Work.

The Statement of Work should be a series of relatively short statements that outline, step-by-step, how each of the major goals or objectives of the proposed research will be accomplished. As appropriate, the Statement of Work should:

1. Describe the work to be accomplished as tasks (tasks may relate to specific aims),

2. Identify the timeline and milestones for the work over the period of the proposed effort,

3. Indicate the numbers of research subjects (animal or human) for each task,

4. Identify methods, and

5. Identify products/deliverables for each phase of the project.

Complete and submit with your proposal immediately after the table of contents to confirm that all components are included in your application.

Award Checklist for FY00 NFRP Proposal Submission

Yes	No	
☐	☐	**Proposal Cover Booklet (original plus 3 copies)**
☐	☐	**Proposal (original plus 30 copies)**

Original plus 30 copies includes:

☐	☐	Peer Review Referral Page
☐	☐	Proposal Title Page (1-page limit)
☐	☐	Table of Contents (1-page limit)
☐	☐	Checklist for Proposal Submission (1 page)
☐	☐	Technical Abstract (1-page limit)
☐	☐	Public Abstract (1-page limit)
☐	☐	Statement of Work (2-page limit)
☐	☐	Relevance Statement (1-page limit)
		Proposal Body:
☐	☐	Idea (10-page limit)
☐	☐	New Investigator (15-page limit)
☐	☐	Investigator-Initiated Research Award (20-page limit, plus 1-page per trainee for Nested Postdoctoral Traineeships)
☐	☐	Clinical Trial (50-page limit)
☐	☐	Abbreviations (1-page limit)
☐	☐	References (no page limit)
		Biographical Sketches (3-page limit per individual):
☐	☐	Applicant
☐	☐	Key Personnel
☐	☐	Existing/Pending Support (no page limit)
☐	☐	CDMRP-Sponsored Research Progress Report (3-page limit per PI)
☐	☐	Facilities/Equipment Description (no page limit)
		Administrative Documentation:
☐	☐	Letters from Collaborating Individuals and/or Institutions (if applicable)
☐	☐	Statement of Eligibility Form (New Investigator and Nested Postdoctoral Traineeships)
☐	☐	*Detailed Cost Estimate (no page limit)*
☐	☐	Budget Justification
☐	☐	Total cost estimate matches Proposal Cover Booklet item 4
☐	☐	Instruments (no page limit)
☐	☐	Publications and Patent Abstracts (5-document limit)
		Appendix H Institutional Review Board (IRB) Documentation
☐	☐	All clinical research proposals involving human subjects and/or human anatomical substances must comply with the requirements detailed in Appendix H before proposals are programmatically reviewed. IRB documentation from the primary submitting institution may be submitted with the proposal. Otherwise, this documentation must be received no later than December 28, 2000 at 4:00 p.m. Eastern Time.
		Additional Materials: Submit together in a manila clasp envelope.
☐	☐	Abstracts (2 additional copies Technical plus 2 additional copies Public)
☐	☐	3½" disk containing files of both abstracts
☐	☐	Statement of Work (2 additional copies)

By signing below, you confirm that your proposal contains the information requested above.

_____ _____

Signature of Applicant Date

NOTE: Exceeding page limits may result in proposal rejection prior to peer review.

As a guide, the Statement of Work for a 3-year effort should require approximately 1 page of single-spaced typing. Several sample Statements of Work are included as a reference in Appendix D of this Program Announcement.

In addition to the Statement of Work pages contained within the proposal, submit two additional copies in the manila clasp envelope with the abstracts and disk.

10. Proposal Relevance Statement – Start section on a new page – 1-page limit

In the Proposal Relevance Statement, the investigator should describe how the proposed research is pertinent to one or more critical issues of the disease.

11. Proposal Body – Start section on a new page – page limit depends upon award mechanism

Each award mechanism has specific instructions for the description of the project and page limits. Investigators should refer to the specific evaluation criteria listed under the award mechanism to which they are applying to ensure that the necessary information is included.

12. Abbreviations – Start section on a new page – 1-page limit

Provide a glossary of all acronyms, abbreviations, and symbols used.

13. References – Start section on a new page – No page limit

List all relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

14. Biographical Sketches – 3-page limit per investigator

Biographical sketches should be prepared for each of the key personnel listed on the budget page including collaborating investigators and mentors. Biographical sketches may not exceed 3 pages. The "Biographical Sketch" form can be found in Appendix E, or downloaded from the CDMRP web site at http://cdmrp.army.mil/?/announce/forms. A list of significant publications and a succinct summary of the investigator's professional experience in the disease and/or potential for contribution to the field should be incorporated into the biographical sketch.

15. Existing/Pending Support – No page limit

List on a separate page, the titles, time commitments, supporting agencies, durations, and levels of funding for all existing and pending research projects involving the PI and key personnel. Proposals submitted under this Program Announcement should not duplicate other funded research projects. If no support exists, state "none".

16. CDMRP-Sponsored Research Progress Report – 3-page limit per PI

If the applicant(s) has received previous funding from any programs managed by the CDMRP, please list on a separate page the DAMD award number, proposal title, and PI name. Also, please provide a short synopsis of the research proposal, a bulleted list of key research accomplishments and reportable outcomes. Reportable outcomes include: manuscripts, abstracts, presentations, patent and licenses applied for and/or issued, animal models, development of cell lines, and infomatics such as databases. **Note: This section is not for additional data, figures, or other similar information relevant to the current proposal submission.**

17. Facilities/Equipment Description – No page limit

Describe the facilities available for performance of the proposed research. Describe the institutional commitment including any additional facilities or equipment proposed for acquisition or available for use at no cost to the USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use.

18. Administrative Documentation – No page limit

Provide letter(s) from proposed collaborating individuals or institutions confirming collaborative efforts that are necessary for the project's success. Other support documentation also may be required within specific award categories. Please follow specific instructions in each award mechanism. **Note: This section is not for additional data, figures, or other similar information.**

19. Detailed Cost Estimate – No page limit

Budget is a key consideration in both peer and programmatic review; applicants are cautioned to use discretion in budget requests. Use the Detailed Cost Estimate form to prepare a detailed cost estimate of the proposed research. This form can be found in Appendix F, or downloaded from the CDMRP web site http://cdmrp.army.mil/?/announce/forms. The cost of preparing proposals in response to this Program Announcement is not considered an allowable direct charge to any resultant award.

20. Instruments – No page limit

Attach questionnaires, survey instruments, or clinical protocols as they apply to the proposal.

21. Publications and Patent Abstracts – 5-document limit

Include up to five relevant publication reprints and patent abstracts. A patent abstract should provide a nonproprietary description of the patent application. If more than five such items are

included in the submission, **the extra items will not be forwarded to peer review.** Every copy of your proposal must include the same reprints and patent abstracts submitted with the original proposal.

22. Proposal Submission

Submit the following documentation to the address listed in the Foreword under Proposal Submission:

Proposal:	**ONE** clearly labeled original (binder-clipped) and **THIRTY** collated photocopies (stapled or binder-clipped) of the **entire package. Every copy must match the original including reprints of any publications.** Do not use rubber bands, or spiral or three-ring binders.
Proposal Cover Booklet:	**ONE** original (binder-clipped to the original proposal) and **THREE** photocopies (**not** binder-clipped to proposal copies).
Letters of Recommendation:	If required, binder-clipped to the front of the original proposal under the original Proposal Cover Booklet. See individual application instructions.
Abstract Pages:	**TWO** additional copies of both the technical and the public (nontechnical) abstracts in a manila clasp envelope along with a 3½" computer disk containing the abstract files (clearly labeled with the name of the PI, institution, and word processing program). Format abstracts in Word, WordPerfect, or ASCII.
Statement of Work:	**TWO** additional copies of the Statement of Work in the same manila clasp envelope with abstract copies and disk.
Packaging:	Package only **ONE** complete proposal submission (original plus all copies requested above) per box. If acknowledgment of proposal receipt is desired, enclose a self-addressed, stamped postcard with each submission. This postcard should state the proposal title and PI's name.
Noncompliance:	Noncompliance to established guidelines may be perceived as an attempt to gain an unfair advantage and may therefore result in proposal rejection. Administrative reasons for **rejection** of all or part of proposals most frequently result from **failure to adhere to timelines, page limits, and font requirements.**

Submit the Proposal to: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP00-Program Announcement)
1076 Patchel Street (Building 1076)
Fort Detrick, MD 21702-5024

23. Receipt Deadline

Deadlines for individual award mechanisms solicited in this Program Announcement are listed in the Foreword and under each award mechanism section.

Any proposal received by the USAMRMC after the exact date and time specified for receipt shall **not** be considered unless it is received before fiscal year 2000 award negotiations have been completed, and:

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

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

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

4. The Government, at its sole discretion, decides to accept the late proposal if it determines that no competitive advantage has been conferred and that the integrity of the competitive grants process will not be compromised.

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

24. Institutional Review Board (IRB) Documentation – To be submitted no later than December 28, 2000 at 4:00 p.m. Eastern Time

All investigators submitting clinical research proposals involving human subjects and/or human anatomical substances must comply with the requirements detailed in Appendix H (Research Involving Human Subjects and/or Anatomical Substances). This documentation can be submitted at the same time the research proposal is submitted but must be received no later than **December 28, 2000 at 4:00 p.m. Eastern Time**.

If IRB documentation is submitted after the proposal is submitted, this information must be sent to the address listed below:

Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP00-IRB)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

25. Regulatory Compliance and Quality Requirements – To be submitted at a later date

Appendices G (Certificate of Environmental Compliance), I (Research Involving Animals), and J (Safety Program Plan) outline Regulatory Compliance and Quality requirements. This information should be provided by the PI to the USAMRMC immediately upon request but **should not be submitted with the original proposal.**

Appendix C

Proposal Cover Booklet Instructions

You must submit an original Proposal Cover Booklet and three photocopies. Additional Cover Booklets and instructions can be requested via phone, fax, e-mail, or mail at the addresses/ numbers listed below. Please allow sufficient time for delivery by regular mail.

Phone: 301-682-5501
Fax: 301-682-5521
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NFRP00-Program Announcement)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

ATTENTION: In order to facilitate the processing of the proposal, it is extremely important that you read and follow the instructions completely as you are filling out the Proposal Cover Booklet. Take special care to see that the written and bubbled figures match exactly.

Marking Instructions

- Use a No. 2 pencil for bubbles.
- Type or print in block letters in the "nonbubble" areas. (Ink is acceptable.)
- Make solid marks that fill the circle completely.
- Make no stray marks on this form.
- Do not fold or tear form.

Specific Instructions for Completing the Proposal Cover Booklet

1. **Proposal Log Number.** (Leave blank.)

2. **Program Identifier and Award Mechanism.** Fill out with "NFRP-00" and award mechanism abbreviation selected from the list on the next page (e.g., NFRP-00, Idea). The mechanism must be filled out with careful consideration because it will determine, in part, how your proposal will be assigned and evaluated for funding.

Award Mechanism	Mechanism Abbreviations
Idea Award	Idea
New Investigator Award	NIA
Investigator-Initiated Research Award without Nested Postdoctoral Traineeship Award	IIRA-W/O
Investigator-Initiated Research Award with Nested Postdoctoral Traineeship Award	IIRA-W
Clinical Trial Award	CTA

3. **Award Mechanism Code.** Select one of the codes listed below. This must agree with the award mechanism listed in question #2.

Award Mechanism	Mechanism Code
Idea Award	01
New Investigator Award	02
Investigator-Initiated Research Award without Nested Postdoctoral Traineeship Award	03
Investigator-Initiated Research Award with Nested Postdoctoral Traineeship Award	04
Clinical Trial Award	05

4. **Total Funding Requested from the Government.** Fill in the total dollar amount requested. This figure is inclusive of all direct and indirect costs for the entire proposed period of the research as indicated on the last line of page 2 of the Detailed Cost Estimate form. **Please be sure to include only the costs requested from the Government.** Do **not** include, in this figure, the amount the institution is willing to cost-share. Enter the amount in whole U.S. dollar figures only, and enter the numbers **flush** with the right-hand margin.

5. **Proposal Title.** Enter the title of the proposal, which may contain up to 160 characters. Capitalize the initial word and the first letter of each subsequent word, with the exception of prepositions, conjunctions, and articles. Please count each blank space as equivalent to one character.

6. **Principal Investigator (PI) Last Name, First Name, and Middle Initial.** The PI is the individual who is primarily responsible for the proposed research.

7. **Title.** Select the appropriate title for the PI.

8. **Degree(s) of Principal Investigator.** Select all that apply.

9-16. **Principal Investigator's Mailing Address.** This is the primary address used to contact the PI. This is the address where the work will be performed. **Do not use the PI's home address, and if possible, avoid the use of PO Boxes.** If applicable, indicate the PI's organization (question #9), department (question #10), then street address (questions #11 and #12). Do not use abbreviations or acronyms of any kind in the address. Do not use

formal terms such as "The" or "The Trustees of" when indicating the organization. **When an organization or department name is not applicable, leave these sections blank and then fill out the PI's address, city, state, country, and zip code in the designated sections.** Applicants should use the appropriate country code listed below for question #15. International applicants should enter the international postal code in the space provided in question #16.

Country	Code	Country	Code	Country	Code
Argentina	AR	India	IN	Senegal	SN
Australia	AU	Indonesia	ID	Singapore	SG
Austria	AT	Ireland	IE	Slovakia	SL
Belgium	BE	Israel	IS	South Africa	ZU
Brazil	BR	Italy	IT	Spain	ES
Canada	CA	Jamaica	JM	Sri Lanka	CE
Chile	CL	Japan	JP	Sudan	SD
China	CN	Kenya	KE	Sweden	SE
Colombia	CO	Korea	KR	Switzerland	CH
Congo	CG	Korea, P.D.R.	KP	Taiwan	TW
Costa Rica	CR	Lebanon	LB	Thailand	TH
Czech Rep	CS	Malaysia	MY	Trinidad/Tobago	TD
Denmark	DK	Mexico	MX	Turkey	TR
Egypt	EG	Netherlands	NL	Uganda	UG
Finland	FI	New Zealand	NZ	United Kingdom	GB
France	FR	Norway	NO	United States	US
Germany	GY	Peru	PE	Uruguay	UY
Ghana	GH	Philippines	PH	Venezuela	VE
Greece	GR	Portugal	PT	Virgin Islands	VI
Guatemala	GT	Puerto Rico	RQ	West Africa	ZW
Iceland	IL	Russia	RU		

17-18. **Principal Investigator's Phone and Fax Numbers.** U.S. and Canada phone and fax numbers must be filled in completely. International phone and fax numbers, including city code and country code, should be indicated in the spaces provided.

19. **Principal Investigator's E-Mail Address.** If the PI has access to e-mail, write the address in the space provided.

20. **Principal Investigator Demographics.** (Optional.) Indicate the PI's gender, ethnicity, and U.S. military affiliation.

21. **Key Personnel Demographics.** (Optional.) Select all that apply for key personnel's gender, ethnicity, and U.S. military affiliation.

Note: The data in questions #20 and #21 are being collected for demographic purposes and will be reported outside the Department of Defense only as grouped data without personal identifiers. Disclosure of this information is voluntary.

22. **Work Performed in a U.S. Military Facility.** Please indicate yes, if some or all of the work will be performed at a Department of Defense, Veterans' Administration, a U.S. Uniformed Health Service institute, or other similar facility.

23. **Human Subjects.** Indicate all human subjects that will be used in this study. If no human subjects will be used, mark the appropriate bubble.

24. **Human Anatomical Substances.** Indicate all human anatomical substances that will be used in this study. If no human anatomical substances will be used, mark the appropriate bubble.

25. **Human Anatomical Substances Traceable to Donors.** Indicate whether human anatomical substances can be traced to a specific donor.

26. **Data Collection from Human Subjects.** Indicate all methods of data collection from human subjects that will used in this study. If no data collection from human subjects will be used, mark the appropriate bubble.

27. **Clinical Trials.** Indicate all of the types of clinical trials that are in the proposed work. If no clinical trials are proposed in this study, mark the appropriate bubble.

28. **Animal Subjects.** Indicate if animal subjects will be used in the proposed work and if animal subjects will be used by a subcontractor.

29. **Safety Provisions.** Select all that apply.

30-35. **Demographics of Human Test Subjects/Study Population of Interest**. If human subjects are being used, you **must** complete all these questions. If human subjects are **not** being used, leave questions 30 to 35 blank. For gender (question #30), demographics (question #31), ethnicity (question #32), age (question #33), general income (question #34), and U.S. military affiliation (question #35) indicate the appropriate descriptors for the human test subjects/study population that are being **specifically** targeted in the proposed research.

36. **Mentor Name.** For Nested Postdoctoral Traineeship proposals only. All Nested Postdoctoral Traineeship proposals **must** include the full name of the mentor. The mentor is the individual responsible for overseeing the training of the trainee listed as the PI on this proposal. If this proposal is not a Nested Postdoctoral Traineeship, leave blank.

37. **Proposal Descriptors - Research Classification.** Choose **ONE** research classification from the following list that best describes the proposed work.

Research Classification	Code
Behavioral/Psychosocial Research	10
Clinical Research	20
Clinical Trials	30
Epidemiology/Public Health Research	40
Laboratory Research	50

38-46. **Proposal Descriptors.** (Leave Blank.)

47. **Administrative Representative Authorized to Conduct Negotiations.** Indicate the primary and secondary administrative contacts authorized to conduct negotiations on the PI's behalf. The organization, address, and appropriate contact information should be provided. The organization listed is the organization that is submitting the proposal on the PI's behalf. If the organization has a Grants/Contracts/Business Official, this is the individual authorized to negotiate potential awards. The signature of an institutional representative certifies that the institution has examined the PI's credentials and verifies that the PI is qualified to conduct the proposed study and to use humans or animals as research subjects, if appropriate. **This signature is mandatory.** For Certifications and Assurances, refer to the U.S. Army Medical Research Acquisition Activity web site located at http://www-usamraa.army.mil, select "Assistance Agreements, Assistance Package Certifications and Assurances."

48. **Organization Code.** (Leave blank.)

49. **Type of Organization.** Choose one organization code that best describes your institution from the list below. Refer to the updated list of Department of Education-recognized Historically Black Colleges and Universities/Minority Institutions (HBCU/MI) to determine HBCU/MI status. This list can be accessed via the CDMRP web site at http://cdmrp.army.mil/?/announce/minority.

Type of Organization	Organization Code
Business-Large	A
Business-Small/Disadvantaged	B
Business-Small/Woman-Owned	C
Business-Small/Other	D
Educational Institution-HBCU	E
Educational Institution-MI	F
Educational Institution-Other	G
Federal Government-Air Force	H
Federal Government-Army	I
Federal Government-Navy	J
Federal Government-Veterans Affairs	K
Federal Government-DOD	L
Federal Government-Other	M
Foreign (non-U.S.)	N

Nonprofit ..... O
Other Organization ..... P
State Government ..... Q

50. **Institution's Official Proposal Control Number.** This is the number that the institution uses to track the proposal. This number, if available, should be provided by the institution's Grants/Contracts/Business office listed in question #47.

51. **Principal Investigator.** The PI must fill out this information and sign in the space indicated. **This signature is mandatory.**

52. **How Did You Hear about This Announcement?** Please indicate all sources from the following list that apply to this announcement.

Source	Code
CDMRP web site	A
CDMRP e-mail	B
CDMRP postcard mailing	C
Previously applied/watched for release date	D
Information from a colleague	E
Science Advertisement	F
Commerce Business Daily Advertisement	G
Advertisement in another technical journal	H
Advertisement in a technical meeting's proceedings	I
Display at American Association of Cancer Research meeting	J
Display at Society of Behavioral Medicine meeting	K
Display at Federation of American Society of Experimental Medicine meeting	L
Display at Minority Health Professionals meeting	M
Display at American Urological Association meeting	N
Display at American Society of Clinical Oncology meeting	O
Display at Complementary and Alternative Medicine meeting	P
Display at Endocrine Society meeting	Q
Display at Gynecology Oncology Group meeting	R
Display at American Society of Human Genetics meeting	S
Display at the Society for the Advancement of Chicanos and Native Americans in Science meeting	T
Display at American Society for Therapeutic Radiology and Oncology meeting	U
Display at Association of Military Surgeons of the United States meeting	V
Display at neurofibromatosis organization meetings, their web sites, or publications	W

Appendix D

Sample Statements of Work

JONES, R.E.

Statement of Work

Development of Peptide Inhibitors of the "Cancer" Receptor (CR)

Task 1. To identify the minimal region of the CR polypeptide able to inhibit intact CR when co-expressed in cultured cells (Months 1-18):

a. Develop a series of plasmids for expressing the CR open reading frame (Months 1-7).
b. Perform assays to ascertain which fragments of CR block DNA-binding (Months 7-18).
c. Confirm that fragments of the CR open reading frame that block DNA-binding activity also inhibit CR function *in vivo* (Months 18-24).

Task 2. To identify short peptides modeled after the receptor that act as inhibitors of DNA binding and subunit association (Months 18-36):

a. Obtain synthetic CR peptides (Months 18-21).
b. Test the effect of synthetic peptides on the DNA-binding activity of CR (Months 20-24).
c. Characterize the inhibitory potency of active peptides and attempt to optimize the effect by testing additional overlapping peptides (Months 21-36).
d. Perform feasibility experiments to assess the ability of selected peptides to inhibit CR function in cultured cells (Months 20-36).

WILSON, JOHN R.

Statement of Work

Ultrasound Imaging

Task 1. Modification of ultrasound imaging gantry, Months 1-12:

a. Modify imaging gantry to permit measurements of the optics.
b. Perform measurements using a multi-modal scanning configuration.
c. Design of final optics.

Task 2. Extensive evaluation of ultrasound imaging gantry with the final optics, Months 13-36:

a. Repeat measurements using the final optics.
b. Measure the contrast improvement provided by the new detector configuration relative to conventional detector configuration.
c. Conduct specimen experiments to evaluate the increase in resolution provided by the magnification.
d. Investigate the extent of artifacts in fixed and scanning modes.
e. Participate in design of a clinical evaluation study comparing modified ultrasound mammography with conventional mammography.

YOUNG, SUSAN D.

Statement of Work

Follow-up Care for Men and Women with Cancer

Task 1. Develop Plan for Follow-up Patient Interviews, Months 1-3:

a. The tracking system shell from the previous cancer project will be modified to track patient recruitment and contact process.
b. The follow-up patient interview will be pre-screened with cancer patients from our hospital who are not enrolled in our study and modifications will be incorporated.
c. The environmental process interview (EPI) used for the baseline interview will be adapted for the follow-up interview.
d. Institutional Review Board approval will be obtained from all hospital sites.
e. The patient interviewer will be trained in medical terminology, measures of the interview, and use of the modified EPI system.

Task 2. Preparation for Medical Record Abstractions, Months 3-9:

a. The Medical Record Abstract form will be finalized and the investigator trained to perform patient data reviews using the instrument.
b. The Medical Record Abstract form will be revised for direct computer data entry.

Task 3. Subject Recruitment and Data Collection, Months 9-20:

a. Patients enrolled in our previous study will be recruited for the proposed follow-up study.
b. Interviews subsequent to the first follow-up will be modified as necessary to reflect issues relevant to patients beyond the period of adjuvant therapy.
c. Surveys will be sent to and data collected from enrolled patients every 6 Months.

Task 4. Abstraction of Medical Records, Months 12-24:

a. Medical record abstractions will be performed for surviving enrolled patients annually.
b. Data entry and quality control measures will be ongoing.
c. Follow-up interviews will be conducted once annually with surviving enrolled patients over the 4-year study period.

Task 5. Interim Analyses, Months 24-44:

a. Interim statistical analyses of data obtained from interviews and medical record abstractions will be performed periodically.
b. Annual reports will be written.

Task 6. Final Analyses and Report Writing, Months 44-48**:**

a. Final analyses of data from interviews and medical record abstractions will be performed.
b. A final report and initial manuscripts will be prepared.

Appendix E

Biographical Sketches

Provide the following information for the key personnel listed on page 1 of the Detailed Cost Estimate form (see Appendix F) for the initial budget period.

NAME	POSITION TITLE

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds 2 pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY.
DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY.
DO NOT EXCEED 3 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Appendix F

Detailed Cost Estimate Form Instructions

The following sections describe the categories of costs that should be recorded on the Detailed Cost Estimate form. All amounts entered should be in U.S. dollars.

Table of Contents

1. Personnel

Show projected salary amounts in terms of annual salary and percentage of effort on the project to be charged by the principal investigator (PI), co-investigator(s), research associate(s), and assistant(s), and the total amount per year to be paid to each staff member of the project. Starting with the PI, list the names of all employees of the applicant who will be involved in the project during the initial budget period, regardless of whether salaries are requested. Include all collaborating investigators, individuals in training, and support staff. Only **ONE** person may be identified as the PI of the proposal.

The qualifications of the PI and the amount of time that he/she and other senior professional key personnel will devote to the research are important factors affecting the selection of research proposals for funding. Awards may be terminated when the PI severs connections with the organization or is unable to continue active participation in the research. Investigators are cautioned that awards are made to institutions. Should the PI of a funded project leave the recipient institution, both the PI and an official of the recipient institution should notify the U.S. Army Medical Research Acquisition Activity prior to leaving the recipient institution to discuss any options available for continued support of the research project.

- **Role on Project:** Identify the role of each individual listed on the project. Describe their specific functions in the "Justification" section (page 3 of the Detailed Cost Estimate form).

- **Type of Appointment (Months):** List the number of months per year reflected in an individual's contractual appointment with the offering organization. The Department of Defense (DOD) staff assumes that appointments at the applicant organization are full time for each individual. If an appointment is less than full time, e.g., 50 percent, note this with an asterisk (*) and provide a full explanation in the "Justification" section (page 3 of the Detailed Cost Estimate form). Individuals may have split appointments (e.g., for an academic period and a summer period). For each appointment, identify and enter the number of months on separate lines.

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

- **Percentage of Effort on Project:** For each key staff member identified on the budget form, list the percentage of each appointment to be spent on this project.

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

- **Fringe Benefits:** Fringe benefits may be requested in accordance with institutional guidelines for each position, provided the costs are treated consistently by the applicant organization as a direct cost to all sponsors. A copy of the rate agreement or other documentation to support the fringe benefits should be provided.

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

2. Consultant Costs

Regardless of whether funds are requested, provide the names and organizational affiliations of all consultants, other than those involved in consortium arrangements.

3. Major Equipment

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

4. Materials, Supplies, and Consumables

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

5. Travel Costs

List the number of trips, destinations, and purposes for all proposed travel. Estimate round-trip travel fare and per diem costs for each trip. Travel to scientific meetings requires identification of the meeting and purpose. The amount allotted for travel is $1,800 per year. The amount allotted for Postdoctoral Trainee travel is $1,500 per year. Itemize travel requests and justify time in the "Justification" section (page 3 of the Detailed Cost Estimate form).

6. Research-Related Patient Costs

Itemize costs of patient participation in the research study. These costs are strictly limited to expenses specifically associated with the proposed study. The U.S. Army Medical Research and Materiel Command will not provide funds for ongoing medical care costs that are not related to a subject's participation in the research study.

7. Other Expenses

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

8. Consortium Costs

A description of services or materials that are to be awarded by subcontract or subgrant is required. For awards totaling $10,000 or more, provide the following specific information:

a. The identification of the type of award to be used (e.g., cost reimbursement and fixed price);

b. If known, the identification of the proposed subcontractor or subgrantee and an explanation of why and how the subcontractor or subgrantee was selected or will be selected;

c. Whether the award will be competitive and, if noncompetitive, rationale to justify the absence of competition; and

d. The proposed acquisition price.

9. Indirect Costs (overhead, general and administrative, and other)

The most recent rates, dates of negotiation, base(s), and periods to which the rates apply should be disclosed along with a statement identifying whether the proposed rates are provisional or fixed. A copy of the negotiation memorandum should be provided.

Training awards frequently have a different institutional overhead charge. All training investigators are encouraged to check with their institution concerning overhead costs.

10. Total Costs for the Entire Proposed Period of Support (second page of the Detailed Cost Estimate form)

Enter the totals under each budget category for all additional years of support requested and itemize these totals in the "Justification" section (page 3 of the Detailed Cost Estimate form). **Note with an asterisk (*) and explain any significant increases or decreases from the initial year budget. Also, explain any escalations of the budget from the initial to the future year(s) of support.** All amounts should be in U.S. dollars. Total costs for the entire proposed period of support on the last line of page 2 should agree with the amount entered in item 4 of the Proposal Cover Booklet (Bubble Sheet) (see Appendix C).

11. Justification (third page of the Detailed Cost Estimate form)

Each item in the budget should be clearly justified under the "Justification" section (page 3 of the Detailed Cost Estimate form). In addition, for projects with a substantial foreign component, explain and justify this on the "Justification" page.

Detailed Cost Estimate Form

Name of Principal Investigator *(last, first, middle)*

DETAILED BUDGET FOR INITIAL BUDGET PERIOD					**FROM**		**THROUGH**
PERSONNEL		**TYPE APPT. (MONTHS)**	**ANNUAL BASE SALARY**	**% EFFORT ON PROJECT**	**DOLLAR AMOUNT REQUESTED (OMIT CENTS)**		
NAME	**ROLE ON PROJECT**				**SALARY REQUESTED**	**FRINGE BENEFITS**	**TOTALS**
	Principal Investigator						
SUBTOTALS →→→→→							**$**
CONSULTANT COSTS							
MAJOR EQUIPMENT (ITEMIZE)							
MATERIALS, SUPPLIES, AND CONSUMABLES (ITEMIZE BY CATEGORY)							
TRAVEL COSTS							
RESEARCH-RELATED PATIENT COSTS							
OTHER EXPENSES (ITEMIZE BY CATEGORY)							
SUBTOTAL OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD →→→→→							$
CONSORTIUM COSTS	**DIRECT COST**						
	INDIRECT COST						
TOTAL PERSONNEL AND OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD							$
TOTAL INDIRECT COSTS FOR INITIAL BUDGET PERIOD							$
TOTAL COSTS FOR INITIAL BUDGET PERIOD							$

Name of Principal Investigator *(last, first, middle)*

BUDGET FOR ENTIRE PROPOSED PERIOD OF SUPPORT							
BUDGET CATEGORY TOTALS*		**INITIAL BUDGET PERIOD** (FROM FORM PAGE 1)	**ADDITIONAL YEARS OF SUPPORT REQUESTED**				**TOTAL**
			2nd	**3rd**	**4th**	**5th**	
PERSONNEL							
FRINGE BENEFITS							
CONSULTANT COSTS							
MAJOR EQUIPMENT							
MATERIALS, SUPPLIES, AND CONSUMABLES							
TRAVEL COSTS							
RESEARCH-RELATED PATIENT COSTS							
OTHER EXPENSES							
SUBTOTAL DIRECT COSTS							
CONSORTIUM COSTS	**DIRECT**						
	INDIRECT						
TOTAL DIRECT COSTS							
TOTAL INDIRECT COSTS							

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PERIOD OF SUPPORT	**$**
TOTAL INDIRECT COSTS FOR ENTIRE PROPOSED PERIOD OF SUPPORT	**$**
TOTAL COSTS FOR THE ENTIRE PROPOSED PERIOD OF SUPPORT **THIS AMOUNT SHOULD AGREE WITH THAT ENTERED ON THE PROPOSAL COVER BOOKLET, ITEM 4**	**$**

* **Itemize all budget categories for additional years on the Justification page that follows.**

JUSTIFICATION: FOLLOW THE BUDGET JUSTIFICATION INSTRUCTIONS EXACTLY. USE CONTINUATION PAGES AS NEEDED.

Appendix G

Certificate of Environmental Compliance

The Certificate of Environmental Compliance should be executed by the institution's official responsible for environmental compliance.

The Council on Environmental Quality (CEQ) regulations (40 CFR 1500-1508) that implement the National Environmental Policy Act (PL 91-190, as amended) require all federal agencies to examine possible environmental consequences of their proposed and ongoing actions.

The U.S. Army Medical Research and Materiel Command (USAMRMC) examines all medical research and development projects, whether inside or outside the United States, for their potential environmental impacts. In most cases, awardees conducting research in established laboratories that are in compliance with environmental laws and regulations, or are already covered by existing environmental documentation, will not be required to provide additional information about the environmental impact of their proposed research. Such projects will receive a "categorical exclusion" according to the Army regulations that implement the CEQ regulations (AR 200-2). After a proposal has been selected for award, the USAMRMC will determine if a categorical exclusion is warranted. If there are any extraordinary circumstances surrounding the research (e.g., research that involves the transfer of recombinant DNA molecules into the genome of one or more human subjects, requires Biosafety Levels 3 and 4, or uses animals captured from the wild), further information may be requested from the investigator to determine the environmental impact of the proposed research. This information should be submitted in a timely manner in order to receive an award.

Certificate of Environmental Compliance

The offeror currently ☐ IS ☐ IS NOT (check appropriate category) in compliance with applicable national, state, and local environmental laws and regulations. (If not in compliance, attach details and evidence of approved mitigation measures.)

The offeror has examined the activities encompassed within the proposed action entitled

"_____

_____"

(enter title and principal investigator's name), for compliance with environmental laws and regulations. The offeror states that the conduct of the proposed action:

1. WILL NOT violate any applicable national, state, or local environmental law or regulation, and

2. WILL NOT have a significant impact on the environment.

The offeror agrees that if the work required under the proposed action at any time results in a significant impact on the environment or a violation of any applicable environmental law or regulation, the offeror will immediately take appropriate action, to include notifying and/or coordinating with the appropriate regulatory agencies as required by law and notifying the Grants Officer.

_____	_____
Name of Official Responsible for Environmental Compliance	Signature
_____	_____
Title	Date
_____	
Name of Organization	

Appendix H

Research Involving Human Subjects and/or Human Anatomical Substances

Appendix H of this Program Announcement contains the required approvals, forms, and descriptions for research involving human subjects and/or human anatomical substances (including human organs, tissues, cells, body fluids from human subjects as well as graphic, written, or recorded information derived from human subjects). Specific guidelines are subject to change as governing regulations; policies and procedures are updated. Consult "Guidelines for Research Involving Human Subjects and/or Anatomical Substances" at http://mrmc-www.army.mil/rcq/hspd.htm for additional information and updates.

All investigators submitting clinical research proposals to the Neurofibromatosis Research Program involving human subjects and/or human anatomical substances must comply with the requirements detailed in this Appendix before proposals are programmatically reviewed. Institutional Review Board (IRB) documentation from the primary submitting institution must be received no later than December 28, 2000 at 4:00 p.m. Eastern Time.

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Research Involving Human Subjects and/or Human Anatomical Substances

1. Introduction

In 1991, the Department of Defense (DOD), together with 15 other federal agencies, adopted regulations that are known collectively as the Common Federal Rule. These regulations embody the ethical principles of the Belmont Report. Title 32 Code of Federal Regulations Part 219 (32 CFR 219), "Protection of Human Subjects," applies to all research involving human subjects conducted or supported by the DOD. The Department of Health and Human Services (DHHS) National Institutes of Health corollary is 45 CFR 46. Research conducted or funded by the U.S. Army Medical Research and Materiel Command (USAMRMC) is also governed by Army Regulation (AR) 70-25, January 1990 and Office of the Surgeon General (OTSG) Regulation 15-2, January 1989. The USAMRMC also adheres to the Food and Drug Administration (FDA) regulation, Title 21 Code of Federal Regulations for research involving investigational drugs or devices. The OTSG maintains the overall responsibility for protecting human research subjects for the Department of the Army .

2. Definitions

2-a. Research

In the Common Federal Rule, "research" is defined as "...a systematic investigation, including research development, testing and evaluation designed to develop or contribute to generalizable knowledge" (32 CFR 219.102). Activities that meet this definition constitute research for purposes of this policy, whether they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities.

The FDA defines "clinical investigation" as "...any experiment in which a drug is administered or dispensed to, or used involving one or more human subjects..." (21 CFR 312.3). This definition applies to research involving the use of FDA regulated products.

2-b. Human Subjects

In the Common Federal Rule, "human subject" is defined as "a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information" (32 CFR 219.102). This regulation applies to the use of human organs, tissues, cells, or body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects.

The FDA defines "human subject" as "a human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease." (21 CFR 312.3).

3. Human Subjects Research Review Board

3-a. Review Levels

In addition to first level of review and approval by the local IRB, the OTSG requires a second level of review and approval by its Human Subjects Research Review Board (HSRRB) of all research funded by the U.S. Army involving human subjects. HSRRB approval must be obtained prior to initiation of the research protocol.

The HSRRB is functionally similar to a civilian IRB. The HSRRB is supported administratively by the Human Subjects Protection Branch of the Office of the Deputy Chief of Staff for Regulatory Compliance and Quality, USAMRMC.

If your research proposal is recommended for funding and the research involves human subjects, it will determined whether your research is:

1. Exempt from HSRRB review,

2. Eligible for expedited review,

3. No greater than minimal risk and, therefore, can be administratively reviewed and approved by the Acting Chair, HSRRB, or

4. Greater than minimal risk and, therefore, requires full HSRRB committee review.

3-b. Timelines and Outcomes

Research protocols that pose greater than minimal risk to subjects are submitted after local IRB approval through the Human Subjects Protection Branch to the HSRRB for full committee review and approval prior to implementation of the study. Review and approval by the HSRRB is usually accomplished within 45-90 days after submission of the protocol to the HSRRB. After the protocol is approved, any revisions to the protocol consent form, advertisements, questionnaires, or other related study documentation must be submitted through the local IRB to the HSRRB for approval prior to implementation. The Surgeon General of the U.S. Army must approve the recommendations of the HSRRB. The HSRRB will make one of the following four recommendations to The Surgeon General:

1. Approval without revisions,

2. Conditional approval contingent upon revisions and/or additional information,

3. Deferral due to substantive concerns about the conduct of the protocol and/or safety of the subjects, or

4. Disapproval.

4. Claim of Exempt Research

4-a. Approval of Exempt Research Involving Human Subjects or Human Anatomical Substances

Certain categories of research are exempt from review by the HSRRB in accordance with Federal guidelines. If your research fits in one or more of these categories, you may request exempt status for your protocol. Your protocol and Claim of Exemption form will be reviewed to evaluate your claim of exemption.

4-b. Exempt Categories

The following list taken from 32 CFR 219.101 details the exemption categories:

1. "Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

    a. research on regular and special education instructional strategies, or

    b. research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless:

    a. information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

    b. any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph 2 of this section, if:

    a. the human subjects are elected or appointed public officials or candidates for public office, or

    b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

5. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

   a. public benefit or service programs,

   b. procedures for obtaining benefits or services under those programs,

   c. possible changes in or alternatives to those programs or procedures, or

   d. possible changes in methods or levels of payment for benefits or services under those programs.

6. Taste and food quality evaluation and consumer acceptance studies,

   a. if wholesome foods without additives are consumed, or

   b. if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture."

4-c. Claiming Exemption

Complete the form in Section 10 of this appendix entitled, "Claim of Exemption from Review by the Human Subjects Research Review Board" to claim exemption for research involving human subjects or anatomical substances.

5. Guidelines for Writing Research Protocols Involving Human Subjects

5-a. Protocol and Protocol Amendment(s)

Before writing the research protocol, investigators must consider the requirements of Title 10 United States Code 980, which are applicable to DOD-funded research. Title 10 United States Code 980 requires that "Funds appropriated to the Department of Defense may not be used for research involving a human being as an experimental subject unless: (1) the informed consent of the subject is obtained in advance; or (2) in the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject is obtained in advance." Furthermore and consistent with the Common Federal Rule for the Protection of Human Subjects, if an individual cannot give his or her own consent to participate in a

research study, consent of the individual's legally authorized representative must be obtained prior to the individual's participation in the research. Moreover, an individual not legally competent to consent (e.g., incapacitated individuals, incompetents, minors) may not be enrolled in DOD-funded research unless the research is intended to benefit each subject enrolled in the study. For example, a subject may benefit directly from medical treatment or surveillance beyond the standard of care. Proposers 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.

Investigational New Drug (IND) or Investigational Device Exemption (IDE) protocols will follow the format described in the International Conference on Harmonisation (ICH), Consolidated Guideline E6 (http://www.ifpma.org/pdfifpma/e6.pdf). Other protocols may follow the ICH Guideline and include applicable paragraphs.

All protocols, to include IND or IDE protocols, must include at a minimum:

1. Project Title. The consent form title must match the project title.

2. Phase. For Food, Drug, and Cosmetic Act regulated medical products, designate as a Phase I, II, III, or IV protocol.

3. Principal Investigator (PI). State the complete name, address, and phone number of the PI. Include a copy of the PI's curriculum vitae (CV) with the protocol.

4. Location of Study. List all centers, clinics, or laboratories where the study is to be carried out. State the complete address and name of the investigator(s) for each site.

5. Time Required to Complete. State the month and year of expected start and completion times.

6. Objectives. Provide a detailed description of the purpose and objectives of the study.

7. Study Population.

    a. Describe the source, number, age range, and gender of subjects together with the inclusion and exclusion criteria.

    b. If pregnant subjects will be excluded from participation in the study, the method of determining pregnancy status in women of childbearing potential must be specified. Also, the time that will elapse between the pregnancy test and exposure to research procedures or medical products must be documented. For IND studies, pregnancy testing is required within 48 hours before the start of the study.

8. Protocol Design. Outline the proposed methodology in sufficient detail to show a clear course of action. Technological reliability and validity of procedures should be indicated. Minimum guidance for the plan should include:

    a. Subject identification (describe code system to be used).

    b. Subject assignment (randomization).

    c. Evaluations prior to entry.

    d. Evaluations to be made during the conduct of the study (i.e., laboratory evaluations, specimens to be collected, schedule and amounts, storage to include where and whether special conditions are required, labeling, and disposition).

    e. Clinical assessments (i.e., schedule of clinical evaluations and follow-up procedures).

9. Risk/Benefits Assessment. Describe the risks associated with the research, precautions to be taken to minimize and/or eliminate risks, and special medical or nursing care that will be needed. Describe benefits of the research to the subject. If there are no benefits, state as such.

10. Reporting of serious and unexpected adverse events.

    a. Include a definition for what constitutes an adverse event in the study.

        i. For IND or IDE research, include definitions as described in 21 CFR 312.32.

        ii. All research protocols must address the following requirements:

            An adverse event temporally related to participation in the study should be documented whether or not considered to be related to the test article. This definition includes intercurrent illnesses and injuries and exacerbations of preexisting conditions. Include the following in all IND safety reports: Subject identification number and initials; associate investigator's name and name of medical facility or Military Treatment Facility; subject's date of birth, gender, and ethnicity; test article and dates of administration; signs/symptoms and severity; date of onset; date of resolution or death; relationship to the study drug; action taken; concomitant medication(s) including dose, route and duration of treatment, and date of last dose.

    b. Describe agencies or offices to be notified in the event of a serious and unexpected adverse event. For investigational new drug or device studies include at a minimum, the following information about reporting serious and unexpected adverse events:

Adverse experiences that are both serious and unexpected must be reported immediately by telephone to the USAMRMC Deputy Chief of Staff for Regulatory Compliance and Quality 301-619-2165 and information faxed to 301-619-7803. A written report must follow the initial telephone call within 3 working days. Address the written report to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RCQ, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

c. Include in adverse event reports the name of the person submitting the report if different from the PI, name of the study, the HSRRB log number (A-xxxx) assigned to the study, the number of subjects enrolled to date, and the number and type of serious and unexpected adverse events previously reported in the study.

d. In addition to the initial report of the adverse event, the report of the medical monitor and a follow-up report describing the resolution of the adverse event need to be provided.

11. Description of Protocol Drug(s) or Devices(s). If the protocol uses an investigational drug or device, provide the following information:

a. IND/IDE number and name of sponsor.

b. Complete names and composition of all medication(s), device(s), or placebo(s).

c. Source of medication(s), device(s), or placebo(s).

d. Location of storage for study medication(s).

e. Dose range, schedule, and administration of test articles.

f. Washout period, if used, should be described in detail.

g. Duration of drug or device treatment.

h. Concomitant medications allowed.

i. Antidotes and treatments available.

j. Disposition of unused drug.

k. The procedure by which the IND sponsor will monitor the protocol in accordance with 21 CFR 312.

l. In addition to the above list of requirements to address in the protocol, include the following with the protocol submission:

(1) A copy of the Investigator's Brochure and/or device manual and associated case report/data collection forms.

(2) For Investigational Devices, include your local IRB's assessment of the risk of the investigational device you plan to use in your study. If the device poses significant risk to research subjects, specify the IDE number obtained from the FDA, the name of the sponsor, and the procedure by which the IND sponsor will monitor the protocol in accordance with 21 CFR 812.

12. Disposition of Data. Describe where data will be stored and duration of storage. Note that records of IND studies must be kept until 2 years after a New Drug Application is approved/ issued, or for 2 years after the IND is withdrawn. Records required for IDE studies should be retained for 2 years after the later of the following dates: the date that investigation is terminated or completed and the date that records are no longer required for support of the premarket approval application.

13. Modification of the Protocol. Describe the procedures to be followed if the protocol is to be modified.

14. Departure from the Protocol. Describe procedures and notifications to be made in the event of deviations from the approved protocol requirements.

15. Roles and Responsibilities of Study Personnel. Briefly describe the duties of study personnel. Include the name of the medical monitor. Duties of the medical monitor are as follows:

    A medical monitor must be assigned to greater than minimal risk protocols. The name and CV of the medical monitor, who is someone other than the PI, must be provided. This individual should be a qualified physician who is not associated with the protocol, able to provide medical care to research subjects for conditions that may arise during the conduct of the study, and able to monitor subjects during the conduct of the study. The medical monitor is required to review all serious and unexpected adverse events associated with the protocol and provide an unbiased written report of the event within 10 calendar days of the initial report. At a minimum, the medical monitor should comment on the outcomes of the adverse event and relationship of the event to the test article. The medical monitor should also indicate whether he/she concurs with the details of the report provided by the PI.

    The medical monitor must forward reports to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RCQ, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

16. Investigators conducting greater than minimal risk research must include the following description of requirements of the Volunteer Registry Database in the consent form:

    It is the policy of the USAMRMC that data sheets are to be completed on all volunteers participating in research for entry into USAMRMC Volunteer Registry Database. The information to be entered into this confidential database includes name, address, social security number, study name, and dates. The intent of the database is two-fold: first, to readily answer questions concerning an individual's participation in research sponsored by USAMRMC and second, to ensure that the USAMRMC can exercise its obligation to ensure

that research volunteers are adequately warned (duty to warn) of risks and to provide new information as it becomes available. The information will be stored at the USAMRMC for a minimum of 75 years.

5-b. Advertisements, Posters, Flyers, or Press Releases to Recruit Subjects

If subjects will be recruited through an advertisement, newspaper article, or similar process, a copy of the local IRB-approved advertisement must be provided.

For studies involving investigational drugs or devices, local IRB review of advertisements is necessary to ensure that the information is not misleading to the subjects participating in IND studies. The FDA has established guidelines on advertisements for subjects. General guidance includes: name and address of PI, summary of research purpose, brief eligibility criteria, truthful list of benefits, and the person to contact for further information.

5-c. Surveys, Questionnaires, or Other Instruments

If the research involves surveys, questionnaires, or other instruments, include a copy of each of these documents with the protocol submission.

6. Informed Consent Requirements

6-a. Elements of Informed Consent

The following information is essential for informed consent documents (32 CFR 219.116 and AR 70-25):

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental.

2. A description of any reasonably foreseeable risks or discomforts to the subject.

3. A description of any benefits to the subject or to others that may reasonably be expected from the research.

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.

6. For research involving more than minimal risk, include the following explanation of medical care available for research-related injury:

Should you be injured as a direct result of participating in this research project, you will be provided medical care, at no cost to you, for that injury. You will not receive any injury compensation, only medical care. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the PI before you enroll in this study.

Three possible mechanisms are available to offset the costs of this requirement:

a. The proposed recipient may absorb such costs into the institution's operating budget.

b. The proposed recipient's liability insurance, if available, may be sufficient to cover any medical care costs. The proposed recipient's business office and/or legal advisor must ensure that there is adequate coverage under this liability insurance.

c. The proposed recipient could negotiate an additional amount of funds, if available, into the award that will cover such medical care cost (such as liability insurance).

7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

6-b. Additional Elements of Informed Consent

When appropriate, one or more of the following elements of information shall also be provided to each subject (32 CFR 219.116 and applicable state/local laws):

1. "A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.

2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

3. Any additional costs to the subject that may result from participation in the research.

4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

6. The approximate number of subjects involved in the study."

7. Documentation of consent for HIV antibody testing, if scheduled, may be addressed in the body of the consent form or as a separate HIV test consent form. Documentation should address any notifications required by local laws as well as any specific issues regarding confidentiality of positive test results.

6-c. Requirements Unique to DOD/USAMRMC-Funded Research

6-c.i. Certification of Translation

Provide documentation that the foreign language version of the consent form is an accurate translation. Documentation should include the following statement, "I certify that this is an accurate and true translation" as well as the signature, name, address, phone number, and if available, fax number of the translator.

6-c.ii. Sample Donation

If the samples donated in this study will be used in other studies, the following statement should be included in the consent form.

> "During this study, you will be asked to provide _____ (clearly specify the type of samples to be provided). These samples will be used for _____ (enter all known and anticipated uses) and may also be used for purposes that are currently unknown. There is a chance that the samples that you are donating under this study may be used in other research studies and may have some commercial value. (If a commercial value is anticipated, that value should be clearly described at this point). Should your donated sample(s) lead to the development of a commercial product, _____ will own it and may take action to patent and license the product. _____ does not intend to provide you with any compensation for your participation in this study nor for any future value that the sample you have given may be found to have. You will not receive any notice of future uses of the sample(s).
>
> (When the study involves treatment as well as research, the following language should be added: "You may agree to participate in the research protocol, but refuse to provide the additional samples discussed above.")
>
> In addition, a donation form may be prepared for signature by the volunteer and a witness that states, "As a participant in _____ (insert the title of the study), I voluntarily donate any and all _____ (clearly specify the type of sample(s) to be provided) to _____. These samples will be used for (enter all known and anticipated uses) and may also be used by _____ for uses not currently known to me. There is a possibility that the samples that I am donating under this study may be used in other research studies and may have some commercial value. (If a commercial value is anticipated, that value should be clearly described at this point). Should my donated sample(s) lead to the development of a commercial product, _____ will own it and it is possible that it will be patented and licensed by _____. _____ does not intend to provide me any compensation for this and will not give me any notice of future uses of my sample(s)."

6-c.iii. Payment for Study Participation: Active Duty Military Personnel

Under 24 USC 30, payment to Active Duty military personnel for participation in research is limited to blood donation and may not exceed $50 per blood draw. Active duty research subjects may not receive any other payment for participation in a research study.

6-c.iv. Confidentiality: Military Personnel

The following statement must be included in the consent form for all protocols that enroll military personnel:

> All data and medical information obtained about you, as an individual, will be considered privileged and held in confidence; you will not be identified in any presentation of the results. Complete confidentiality cannot be promised to subjects, particularly to subjects who are military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities.

6-c.v. Pregnant Women

If pregnant women will be excluded, the following statement must be included if pregnancy during or after the study constitutes a risk to the participant or fetus:

> I should avoid becoming pregnant during the study and for at least (time period in days, weeks, or months) after participation in the study. To avoid becoming pregnant, I should either abstain from sexual relations or practice a method of birth control. Except for surgical removal of the uterus, birth control methods such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm-killing products are not totally effective in preventing pregnancy.

6-c.vi. Volunteer Registry Database

For all studies involving greater than minimal risk, notification regarding the requirements of the Volunteer Registry Database, must be included in the consent form. The U.S. Army Medical Research and Development Command Form 60-R must be completed for each volunteer. Send all completed forms to the Human Subjects Protection Branch annually and at the completion of the study. An example of the form is located in Section 12 of this appendix.

The following statement is normally included in the "Confidentiality" section of the consent form:

> It is the policy of the USAMRMC that data sheets be completed on all volunteers participating in research for entry into this Command's Volunteer Registry Database. The information to be entered into this confidential database includes name, address, social security number, study name, and dates. The intent of the data base is two-fold: first, to readily answer questions concerning an individual's participation in research sponsored by USAMRMC and second, to ensure that the USAMRMC can exercise its

obligation to ensure that research volunteers are adequately warned (duty to warn) of risks and to provide new information as it becomes available. The information will be stored at the USAMRMC for a minimum of 75 years.

7. Assurances

If an institution has a current Multiple Project Assurance (MPA) with the DHHS Office for Protection from Research Risks (OPRR), submit a letter with the following protocol information: (a) MPA number, (b) risk level that the IRB classified the protocol (no greater than minimal risk or greater than minimal risk), (c) date of IRB approval, and (d) next continuing review date. This letter must be on letterhead stationery and signed by the Chairperson of the IRB that approved the protocol.

If the institution does not have a current MPA with OPRR, a written Assurance of Compliance must be filed with the DOD Human Subjects Protection Branch of the Office of the Deputy Chief of Staff for Regulatory Compliance and Quality. The obligation to obtain an assurance can be found in 32 CFR 219.103.

There are four requirements for a DOD Single Project Assurance (SPA) that must be submitted to the Human Subjects Protection Branch. The first is to complete a DOD SPA application. This application can be found at http://mrmc-www.army.mil/rcq/hspd

The second requirement is to provide a table of the IRB membership with the credentials (e.g., MD, Ph.D., etc.) of each member, affiliation with the institute, and the role fulfilled on the IRB (e.g., chairperson, alternate, scientist, etc.). An example of this table is provided in the SPA application.

The third requirement is to provide short CVs or biographical sketches of all IRB members. These CVs are used to verify qualifications of the IRB members. The last requirement is to provide the written procedures that are used by the IRB as outlined in 32 CFR 219.103. The SPA number will be issued after the protocol is approved by the HSRRB.

The fourth requirement is to obtain a letter on letterhead stationery from the Chairperson of the IRB that approved the protocol that must accompany the SPA application. The risk level assigned to the protocol by the IRB must be included along with the date of approval by the IRB and the next continuing review date.

8. Inclusion of Women and Minorities in Research

Consistent with the Belmont Report and recent congressional legislation, special attention is given to the inclusion of women and minorities in research funded by the USAMRMC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. If women and/or minorities will be excluded, a justification must be included.

9. Where to Go for Help and Information

If your research involves human subjects, you should first contact your local IRB for institutional requirements. If you have questions regarding the USAMRMC protocol and consent form requirements or the review and approval process, contact the Office of the Deputy Chief of Staff for Regulatory Compliance and Quality, Human Subjects Protection Branch at the address or phone number listed below.

Phone: 301-619-2166/2165
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-RCQ-HR
504 Scott Street
Fort Detrick, MD 21702-5012

References:

- Title 32 Code of Federal Regulation, Part 219, Protection of Human Subjects
- Title 21 Code of Federal Regulation, Part 50, Protection of Human Subjects
- Title 21 Code of Federal Regulation, Part 56, Institutional Review Boards
- Title 21 Code of Federal Regulation, Part 312, Investigational New Drug Application
- Title 21 Code of Federal Regulation, Part 812, Investigational Devices
- Title 45 Code of Federal Regulation, Part 46, Subparts B,C, and D, Protection of Human Subjects
- Code of Federal Regulations is located at http://www.access.gpo.gov/nara/cfr/index.html
- Army Regulation 70-25, Use of Volunteers as Research Subjects
- Army Regulation 40-7, Use of Investigational Drugs and Devices in Humans and the Use of Schedule I Controlled Drug Substances
- Army Regulations can be located at http://www.usapa.army.mil/gils/epubs1.html
- Office of The Surgeon General Regulation 15-2, Human Subjects Research Review Board
- Title 10 United States Code, Section 980
- Title 24 United States Code, Section 30
- Department of Defense Directive 3216.2
- ICH, Good Clinical Practice, Consolidated Guideline is located at http://www.ifpma.org/pdfifpma/e6.pdf; for all other guidelines, access the ICH homepage at http://www.ifpma.org/ich1

Copies of the preceding references can be obtained from either the U.S. Government Printing Office or the National Technical Information Service at:

U.S. Government Printing Office:
Phone: 202-512-1800
E-mail: www.access.gpo.gov/su_docs
Mail: Superintendent of Documents
P.O. Box 371954
Pittsburgh, PA 15250-7954

National Technical Information Services:	Phone:	703-605-6000; 800-553-NTIS
	E-mail:	orders@ntis.fedworld.gov
	Mail:	National Technical Information Service 5285 Port Royal Road Springfield, VA 22161

10. Claim of Exemption from Review by the Human Subjects Research Review Board

PROTOCOL TITLE:	
PRINCIPAL INVESTIGATOR'S NAME:	PROPOSAL NO:
INSTITUTION:	

1. Will existing or archived data, documents, medical records, or database records be used? Yes No

2. Will biological specimens (e.g., cells, tissues, blood) be used? Yes No

3. Indicate below the sources of existing or archived data or biological specimens or cell lines (e.g., cell lines purchased from ATCC).

_____

_____

4. Will the donors of the original biological specimens be able to be identified, directly or indirectly, through identifiers linked to the donor? Yes No

5. Will data be recorded in writing? Yes No

6. Will data be recorded by audiotape? Yes No

7. Will data be recorded by videotape? Yes No

8. If survey instruments are used, will sensitive or private topics be explored? Yes No

9. Will subjects be identifiable either by name or through demographic data? Yes No

If the answer to any question 4–9 is yes, describe on a separate sheet of paper how the confidentiality of a subject's identity will be maintained. Also describe plans for maintaining or destroying identifying links to subjects after the protocol has been completed.

_____

Principal Investigator's Signature Date

11. Protocol Submission Checklist (Complete the following checklist and submit with your proposal application.)

PROTOCOL TITLE:	
PRINCIPAL INVESTIGATOR'S NAME:	PROPOSAL NO:
INSTITUTION:	

All Protocols:

___ Consent Form(s)

___ If potential commercial use of sample(s) or future use of sample(s) in other studies, a Sample Donation consent form is required.

___ With HIV testing, documentation of consent for HIV antibody testing, if scheduled, may be addressed in the body of the consent form or as separate HIV test consent form.

___ Protocol

___ Curriculum Vitae or Biosketch for Principal Investigator and Medical Monitor

___ Scientific Review/Peer Review Approval(s)

___ Letter from the IRB Chairperson with the following protocol information: (a) MPA number, (b) risk level that the IRB classified the protocol (c) date of IRB approval, and (d) next continuing review date

___ Copy of Recruitment Advertisement(s) and/or Poster(s)

Investigational New Drug (IND) Protocols – additional requirements:

___ Document Specifying IND Number

___ Investigator's Brochure

___ Copy of Case Report Forms (blank)

Medical Device Protocols – additional requirements:

___ Document from manufacturer declaring level of risk for device (nonsignificant risk or significant risk) and IDE form

___ Document Specifying IDE Number

___ Manufacturer's Device Manual/Device Information

Protocol Submission Checklist (cont.)

What type of study is proposed?

___ Phase I Clinical Trial	___ Survey/Medical Record Review	___ Community Intervention
___ Phase II Clinical Trial	___ Cohort (longitudinal study)	___ Laboratory Experiment
___ Phase III Clinical Trial	___ Retrospective (case-control)	___ Tissue Only
___ Multicenter Trial	___ Program/Policy Study	___ Qualitative Study
___ Pilot Study	___ Cross-Sectional (prevalence)	___ Other: _____

Check all procedures applicable to this protocol:

___ Experimental Drug/Medications IND#_____	___ Prosthetic Orthopedic Devices
___ Marketed Agent, but Unapproved Use IND# _____	___ Nutrition/Metabolism Study
___ Experimental Device, IDE# _____	___ Tissue/Organ Transplant
___ Immunological Study	___ Radiation or Radioactive Material
___ Artificial Organ Study	___ Human Embryos
___ Experimental Treatments	___ Diagnostic Procedures
___ Experimental Surgery	___ Anatomical Substances/ Biological Specimens

Other: _____

Drug(s) to be used: _____ Drug Type* _____
_____ _____
_____ _____

*Drug Type may be chosen from the following list or other type may be stated as appropriate:

Analgesics	Anti-cancer drugs	Cardiac drugs	Hematologic agents
Anesthetics	Anti-convulsants	Diuretics	Hormones
Anti-allergy drugs	Anti-hypertensive drugs	Drugs affecting respiration	Tranquilizers/psychotropic drugs
Anti-arrhythmic drugs	Anti-Parkinson agents	Eye/Optical drugs	Vitamins/Minerals
Antibiotics/anti-infective agent	Autonomic drugs	Gastro-intestinal drugs	

Human Subject Information:

Age range of subjects: _____.
Number of subjects expected to be enrolled: Total number of subjects locally _____.
If multicenter study, total number of subjects at all centers _____.

Subject Gender:	___ Male	___ Female	___ Both	___ Non-Consenting Subjects
Subject Age:	___ Infant	___ Child	___ Adolescent	___ Adult ___ Geriatric
Vulnerable Subject Class:	___ Prisoners	___ Minorities	___ HIV +	___ Psychologically Impaired
Subject Recruitment:	___ In-Patients	___ Out-Patients	___ Students/Employees	___ Paid Volunteers

_____

Principal Investigator's Signature Date

12. U.S. Army Medical Research and Development Command Form 60-R

VOLUNTEER REGISTRY DATA SHEET (USAMRDC 60-R)

THIS FORM IS AFFECTED BY THE PRIVACY ACT OF 1974

1. AUTHORITY: 5 USC 301; 10 USC 1071-1090; 44 USC 3101; EO 9397

2. Principal and Routine Purposes: To document participation in research conducted or sponsored by the U.S. Army Medical Research and Materiel Command. Personal information will be used for identification and location of participants.

3. Mandatory or Voluntary Disclosure: The furnishing of the SSN is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide information may preclude your participation in the research study.

PART A - INVESTIGATOR INFORMATION
(To Be Completed By Investigator)

PLEASE PRINT, USING INK OR BALLPOINT PEN

1. Study Number:_____

2. Protocol Title:_____

3. Contractor (Laboratory/Institute Conducting Study):_____

4. Study Period: From:_____/_____/_____ To:_____/_____/_____
DD MM YY DD MM YY

5. Principal/Other Investigator(s) Names(s):
_____
_____
_____

6. Location/Laboratory:
_____/_____
_____/_____
_____/_____

PART B - VOLUNTEER INFORMATION
(To Be Completed By Volunteer)

PLEASE PRINT, USING INK OR BALLPOINT PEN

7. SSN:_____/_____/_____ 8. Name:_____

9. Sex: M___F___ 10. Date of Birth:____/____/____ 11. *MOS/Job Series:_____ 12: Rank/Grade:_____

13. Permanent Home Address (Home of Record) or Study Location:_____
(Street) or (P.O. Box/Apartment Number)

_____
(City) (Country) (State) (Zip Code)

Permanent Home Phone Number:_____

14. *Local Address (If Different From Permanent Address):_____
(Street) or (P.O. Box/Apartment Number)

_____
(City) (Country) (State) (Zip Code)

Local Phone Number:_____

15. *Military Unit: _____ Zip Code:_____

Organization:_____ Post:_____ Duty Phone Number:_____

VOLUNTEER REGISTRY DATA SHEET (USAMRDC 60-R) (continued)

PART C - ADDITIONAL INFORMATION
(To Be Completed By Investigator)

PLEASE PRINT, USING INK OR BALLPOINT PEN

16. Location of Study:_____

17. Is Study Completed: Y:___ N:___

Did volunteer finish participation: Y:____ N:____ If YES, date finished_____/_____/_____
DD MM YY

If NO, date withdrawn:____/____/_____ Reason Withdrawn:_____
DD MM YY

_____

18. Did any Serious or Unexpected Adverse Incident or Reaction Occur: Y:____ N:_____ If YES, Explain:
_____
_____
_____

19. *Volunteer Follow-up:_____

Purpose: _____

Date: ____/____/____ Was contact made: Y:____ N:____ If NO action taken, explain:_____
DD MM YY

_____

20. *Hard Copy Records Retired: Place:_____ File NR:_____

21. *Product Information:

Product:_____

Manufacturer:_____

Lot #:_____ Expiration Date:_____

NDA # _____ IND/IDE #:_____

*Indicates that item may be left blank if information is unavailable or does not apply. Entries must be made for all other items.

When completed, a copy of this form should be sent to the address below:

Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-RCQ-HR
Fort Detrick, MD 21702-5012

Appendix I

Research Involving Animals

Table of Contents

Research Involving Animals

1. Introduction

If using animals, provide all information required by this appendix. Any and all subcontractors using animals must also provide the information required by this appendix.

The Department of Defense (DOD) definition of **animal: Any live nonhuman vertebrate.**

The DOD Directive 3216.1, dated April 17, 1995, provides policy and requirements for the use of animals in DOD-funded research. **These requirements may differ from those of other funding agencies.** Each of the following items **must** be addressed in a proposal appendix entitled "Research Involving Animals." Questions concerning animal use should be directed to:

Phone: 301-619-2144
Fax: 301-619-4165
Mail: U.S. Army Medical Research and Materiel Command
ATTN: MCMR-RCQ-AR
504 Scott Street
Fort Detrick, MD 21702-5012

2. Alternatives to Painful Procedures

A painful procedure is defined as any procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being to which that procedure is applied. A written narrative description of the methods and sources used to search for alternatives to painful procedures, including those procedures in which pain is alleviated, **must** be provided. The minimal written narrative must include: the databases searched or other sources consulted, the date of the search and the years covered by the search, and the key words and/or search strategy used. Where federal law requires specific testing procedures, state the appropriate Code of Federal Regulations or legal guidance that requires this testing. (The U.S. Army Medical Research and Materiel Command [USAMRMC] reserves the right to request evidence that a literature search for alternatives to painful procedures was performed.)

3. Rationale for Using Animals

Provide a rationale for using animals in the proposed research. Explain what alternatives to animal use were considered, such as computer modeling or cell cultures, and explain why these alternatives cannot be used to obtain the research objectives. **It is USAMRMC policy that alternatives to the use of animals be thoroughly investigated prior to submission of any proposal involving animals.**

4. Species Identification and Rationale

Identify the species of animals to be used and provide a rationale for their use. Explain why this particular animal model(s) was chosen over other animal models. Include references to unique biologic or physiologic characteristics that influenced the choice of animal model(s).

5. Rationale for the Number of Animals Required

Provide the **total number of each species of animals** to be used by experimental design. Justify these numbers either **scientifically or mathematically. Show how these numbers were statistically determined to be the minimum** required to obtain valid results.

6. Experimental Design

Provide a complete description of the proposed use of the animals by experimental design. Include surgical procedures, biosamples (frequency, volume, harvest site, and method of tissue collection), adjuvants and other injections (agent, dosage, route, and anatomical site of administration).

7. Anesthesia/Analgesia/Tranquilization

Describe what anesthetics, tranquilizers, and analgesics will be used by agent, dosage, route, and anatomical site of administration. If none are to be used, provide an explanation.

8. Study Endpoint

Describe the projected endpoint or termination of the study for the animals.

9. Euthanasia or Final Disposition

Describe the method of euthanasia by agent, dosage, route, and anatomical site of administration. If animals are not euthanized, state final disposition of the animals.

10. Institutional Animal Care and Use Committee(s) Approval

Provide written documentation of protocol approval from the Institutional Animal Care and Use Committee(s) (IACUC) where the animal research will be performed including any subcontracting facility. If IACUC approval is pending provide a statement to this effect. Evidence of committee review can follow proposal submission, but must be provided prior to award. **RESEARCH WILL NOT BE FUNDED WITHOUT EVIDENCE OF APPROVAL FROM THE IACUC(s).**

11. U.S. Department of Agriculture Animal and Plant Health Inspection Service Animal Care Inspection Report

Include a copy of the most recent U.S. Department of Agriculture Inspection Report for any and all facilities where animal research will be performed, including any subcontracting facility.

12. Qualifications

Provide information on the qualifications and training of personnel performing the animal procedures. It must specifically address the training and experience these personnel possess in using and manipulating the species of animals detailed in the proposal.

13. Accreditation

One of the following must be provided for each facility where animal research will be conducted:

1. Evidence that the facility is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.

2. A copy of the Institutional Letter of Assurance of Compliance with the "Public Health Service Policy on Humane Care and Use of Laboratory Animals," revised September 1986.

3. A statement signed by the Institutional Official that the care and use of animals will be performed according to the National Research Council 1996 "Guide for the Care and Use of Laboratory Animals" and applicable federal regulations.

14. Principal Investigator Assurances

The principal investigator must provide the following signed assurances (this page may be photocopied and signed):

1. I assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research and that analgesic, anesthetic, and/or tranquilizing drugs will be used where indicated and appropriate to minimize discomfort and pain to animals.

2. I assure that the animals authorized for use in this protocol will be used only in the activities, manner, and quantities described herein, unless a deviation is specifically approved by my IACUC and the USAMRMC Animal Care and Use Review Office.

3. I accept full responsibility for the proper care and use of the animals during the conduct of research outlined in the proposal.

4. I verify that I have made a reasonably good faith effort to ensure that this protocol is not an unnecessary duplication of previous experiments.

5. I verify that the personnel performing the animal procedures/manipulations described in this protocol are technically competent in those procedures and have received training on the use of animals in research as required by the Animal Welfare Act of 1985.

6. I assure that I have consulted with an individual who is qualified to evaluate the statistical design or strategy of this proposal and that the minimum number of animals needed for scientific validity will be used.

_____

Principal Investigator's Signature

NOTE: For proposals that require the use of nonhuman primates, companion animals, marine mammals, or for research deemed sensitive by the USAMRMC, a site visit shall be conducted as necessary by the USAMRMC Animal Care and Use Review Officer or designees.

Appendix J

Safety Program Plan

Appendix J of this Program Announcement contains the required assurances, approvals, forms, and descriptions relating to safety in the research environment.

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Safety Program Plan

Each of the applicable items below must be addressed in a proposal appendix entitled "Safety Program Plan" and must be prepared specifically for the proposal. Each item should be research specific and addressed in order. Institutional safety manuals may be referenced; however, **do not send copies of your Safety Manual or Standard Operating Procedures (SOPs).** A list of program contents with a brief description of each item (maximum 3 pages) is acceptable. Provide a web site address, if available, for additional safety information.

Those items that do not apply to the proposed research shall be labeled as "not applicable" or "N/A."

1. Research Operations/SOPs

Identify all safety procedures relating to the research operation. These should include, but are not limited to the following: a description of safety procedures for performing the protocol; a description of any special skills, training, and SOPs that assure safe research operations (Safety Committee, HAZCOM, Bloodborne Pathogen, Chemical Hygiene Plan, etc.); and a description of medical surveillance and support.

2. Facility Equipment and Description

This section should include a description of any safety cabinets and ventilation system employed.

3. Hazard Analysis

Provide a description of each hazard identified, the hazard analysis performed based on maximum credible event, and the plan to minimize or eliminate each hazard.

4. Radioactive Materials

Identify any radioactive materials used and the disposal method for each. A copy of the Nuclear Regulatory Committee or state-approved license shall be submitted with this application.

5. Recombinant DNA

Research involving recombinant DNA must meet or exceed National Institute of Health (NIH) "Guidelines for Research Involving Recombinant DNA Molecules," January 1997 edition. Include a written approval letter from the organization's Institutional Biosafety Committee. If DNA experiments are exempt under the NIH Guidelines, include a copy of the written exemption notification.

Copies of the above NIH Guidelines are available at:

Phone:	301-496-9838
Fax:	301-496-9839
Web site:	www.nih.gov/od/oba
Mail:	Office of Biotechnology Activities National Institutes of Health, MSC 7010 6000 Executive Boulevard, Suite 302 Bethesda, MD 20892-7010

6. Biological Defense Program Requirements

Contractors performing work with **Biosafety Level-3 and -4** material must prepare a safety plan in accordance with 32 CFR 626.18. See www.access.gpo.gov/nara/cfr/index.html for a copy of the 32 CFR.

The principal investigator (PI) is directly responsible and liable for all aspects of research project safety and ensures that all Safety Plan requirements are in compliance with 32 CFR 626 and 627 (Biological Defense Safety Program and The Biological Defense Safety Program, Technical Safety Requirements).

Local emergency support agencies, such as law enforcement, fire departments, health departments, and governments will be informed of Biological Defense Program (BDP) activities and the appropriate support necessary, to include any equipment and training needed to provide effective emergency response. Agreements with external agencies must be formalized. (For the purpose of this requirement, the term "local emergency support agencies" refers to any agency that could reasonably be expected to have some capability to provide timely and effective support in the management or resolution of a biological mishap arising from BDP operations.) **A copy of this agreement must be submitted with the proposal.**

Local Emergency Support
(Sample Form)

(Police, Fire, Health Department), is fully aware of the research program entitled _____ in the Department of _____ at _____, which is supported by the U.S. Army Medical Research and Materiel Command (Contract Number_____). In the event that a situation requires our response, we are equipped and prepared to handle those emergencies as appropriate for this project.

Acknowledged:

_____

Name Title (e.g., Fire Chief) Date

7. Institutional Safety Director/Manager Assurances

- I assure that this institution has an existing institutional safety and occupational health program that meets appropriate federal, state, and local regulations as required by the U.S. Army Medical Research and Materiel Command Safety Office.

- I assure that all hazards described in the proposal have been identified, eliminated, and/or controlled in such a manner to provide for a safe research laboratory environment.

_____ _____

Safety Director/Manager Signature Date

8. Principal Investigator Assurances

The PI must provide the following signed assurances.

- I assure that my institution has an existing safety and occupational health program that meets appropriate federal, state, and local regulations as required by the Occupational Safety and Health Act; that hazards have been identified, eliminated, and/or controlled; and that research may be performed safely under laboratory conditions.

- I assure that I shall adhere to the institutional safety and occupational health program policies and procedures.

- I assure that I will supervise the performance of my laboratory staff to ensure that the required safety practices and techniques are employed.

- I assure that I have involved the institutional safety officer in the planning of this research proposal, discussing all aspects of the proposal that relate to occupational health and safety.

- I understand that I am directly responsible and liable for all aspects of safety and occupational health specific to my research protocol.

_____ _____

Principal Investigator Signature Date

Appendix K

General Information

Appendix K of this Program Announcement contains general information relating to U.S. Army Medical Research and Materiel Command (USAMRMC) policies and procedures.

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General Information

1. U.S. Army Medical Research and Materiel Command Award

The USAMRMC implements its extramural research program predominantly through the award of grants and cooperative agreements. Proposals selected for funding are processed by the U.S. Army Medical Research Acquisition Activity (USAMRAA).

All awards are made to organizations, not individuals. A principal investigator (PI) should submit a proposal through, and be employed by or affiliated with, a university, college, nonprofit research institute, commercial firm, or Government agency (including military laboratories) in order to receive support.

2. Procurement Integrity, Conflicts of Interest, and Other Improper Business Activities

The Procurement Integrity Act, Title 41 U.S. Code 423, et seq., contains prohibitions against certain activities between Offerors and Government officials. Any questions regarding these prohibitions should be directed to the USAMRMC legal staff at 301-619-2065. Proposed military/civilian collaborations should pay special attention to the Procurement Integrity Act.

3. Disclosure of Information Outside the Government

By submission of an application, the applicant understands that disclosure of information outside the Government shall be for the sole purpose of technical evaluation. The USAMRMC will obtain a written agreement from the evaluator that information in the proposal will only be used for evaluation purposes and will not be further disclosed or utilized. Funded projects may be subject to public release under the Freedom of Information Act; proposals that are not selected for funding will not be subject to public release.

4. Award Eligibility

To be eligible for award, a prospective recipient should meet certain minimum standards pertaining to institutional support, financial resources, prior record of performance, integrity, organization, experience, operational controls, facilities, and conformance with safety and environmental statutes and regulations (Office of Management and Budget Circular A-110).

5. Government Obligation

PIs are cautioned that only an appointed Contracting/Grant Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government to fund preparation of a proposal or to support research should be inferred from discussions with a technical project officer. A PI who, or an organization that, makes financial or other commitments for a research effort in the absence of an actual legal obligation signed by the USAMRAA Contracting/Grant Officer does so at their own risk.

6. Information Service

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

7. Funding Instrument

All awards under this Program Announcement are anticipated to be grants or cooperative agreements.

More information on these funding instruments may be obtained by request from:

Fax:	301-619-2937
E-mail:	q&a.baa@det.amedd.army.mil
Mail:	Director U.S. Army Medical Research Acquisition Activity ATTN: MCMR-AAA Fort Detrick, MD 21702-5014

8. Inquiry Review Panel

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

9. Equipment/Property

It is the policy of the Department of Defense that all commercial and nonprofit recipients posses the equipment and facilities needed to support proposed research. In those rare cases when additional specific equipment is approved for commercial and nonprofit organizations, such approved cost elements shall be separately negotiated.

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

Appendix L

Acronym List

AR	Army Regulation
BCRP	Breast Cancer Research Program
BDP	Biological Defense Program
CDMRP	Congressionally Directed Medical Research Programs
CEQ	Council on Environmental Quality
CFR	Code of Federal Regulations
CR	Cancer Receptor
CTA(s)	Clinical Trial Award(s)
CV	Curriculum Vitae
DHHS	Department of Health and Human Services
DOD	Department of Defense
DOEd	Department of Education
EPI	Environmental Process Interview
ET	Eastern Time
FDA	Food and Drug Administration
FY	Fiscal Year
HBCU/MI	Historically Black Colleges and Universities/Minority Institutions
HSRRB	Human Subjects Research Review Board
IACUC	Institutional Animal Care and Use Committee(s)
ICH	International Conference on Harmonisation
IDE	Investigational Device Exemption
IIRA(s)	Investigator-Initiated Research Award(s)
IND	Investigational New Drug
IP	Integration Panel
IRB	Institutional Review Board
MPA	Multiple Project Assurance
NF	Neurofibromatosis
NFRP	Neurofibromatosis Research Program
NIH	National Institutes of Health
OPRR	Office for Protection from Research Risks
OTSG	Office of the Surgeon General
PI	Principal Investigator
SOPs	Standard Operating Procedures
SPA	Single Project Assurance
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRMC	U.S. Army Medical Research and Materiel Command