Announcement of Federal Funding Opportunity

Summary

I. GENERAL INFORMATION

A. Title of Award: Natural History Development Award (NHDA).

B. Program Name: Department of Defense (DOD) Fiscal Year 2005 (FY05) Tuberous Sclerosis Complex Research Program (TSCRP).

C. Funding Opportunity Number: TS05-NHDA.

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

E. Agency Contact(s)

1. Questions related to the Program, proposal format, or required documentation may be addressed to the CDMRP at:

Phone:	301-619-7079
Fax:	301-619-7792
E-mail:	cdmrp.pa@det.amedd.army.mil
Mail:	Commander US Army Medical Research and Materiel Command ATTN: MCMR-ZB-C (TS05-NHDA) 1077 Patchel Street (Building 1077) Fort Detrick, MD 21702-5024

2. Questions related to electronic submission: The help line phone number(s) is 301-682-5507 and is also provided on the Web. Other help desk contact information is:

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

F. Anticipated Instrument Type(s): Grants/Cooperative Agreements.

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

H. Website Address to Access Application Package: Proposals must be submitted electronically at https://cdmrp.org. The website contains all the information, forms, documents, and links needed to apply.

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

II. FUNDING OPPORTUNITY DESCRIPTION

The intent of the Natural History Development Award is to support the development of a **focused, hypothesis-driven** natural history study that will enhance the current knowledge of TSC manifestations and improve clinical management of the disorder and/or the development and clinical testing of new interventions. **Recipients of the Natural History Development Award will be required to submit a proposal, clinical protocol, and informed consent/assent form(s) for the Natural History Study Award in FY06, pending receipt of funds by the TSCRP.**

This mechanism is **not** intended to support descriptive, broad-based proposals that are limited to collecting information (clinical, pathological, radiographical, or other) with no accompanying analysis or hypothesis testing. Instead, proposals must include a specific hypothesis or question regarding the natural history of TSC; detailed plans to develop a study to test the hypothesis or answer the question; and discussion of how the proposed study will improve clinical management and/or facilitate the development of TSC clinical trials. Proposals should outline plans for the establishment of the research team, the development of tools for data management and trial/research administration, the definition of participant recruitment strategies, and the development of the clinical protocol and other essential components of the study included in a Manual of Operations and Procedures.

III. AWARD INFORMATION

- Type of award: grant/cooperative agreement.
- Approximately $0.15 million (M) is available to fund the FY05 TSCRP Natural History Development Awards.
- Depending on the number and quality of the applications, it is anticipated that one proposal will be funded.
- Funding for the FY05 Natural History Development Award can be requested for $150,000 for 18 months, inclusive of both direct and indirect costs. FY05 funding will be disbursed in two installments, one installment of $100,000 at the time of the award and the second installment of $50,000 contingent upon submission of a compliant FY06 Natural History Study Award proposal, clinical protocol, and informed consent form.

- Recipients of the Natural History Development Award will be required to submit a proposal, clinical protocol, and informed consent/assent form(s) for the Natural History Study Award in FY06 according to guidance provided in the TSCRP FY06 Natural History Study Award Program Announcement.
- The FY06 TSCRP is anticipating funding one to two Natural History Study Awards for a total investment of $1M, pending receipt of funds.
- **Please note that there is no guarantee that funds will be available for the subsequent Natural History Study Awards in FY06.**

IV. ELIGIBILITY INFORMATION

A. Applicants: Applicants from all academic levels are eligible to submit proposals. All individuals, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by, or affiliated with, an eligible institution as defined below.

B. Institutions: Eligible institutions include for-profit, nonprofit, public, and private organizations.

C. Cost Sharing: It is expected that institutions will cost share. Please see "Major Equipment" located in Subsection V.G.2.c of the Full Text of Program Announcement for details.

D. Other Eligibility Criteria: Please see the Full Text of Program Announcement description for details regarding duplicate submissions, applications from Historically Black Colleges and Universities/Minority Institutions (HBCU/MI), and administrative compliance issues.

V. PROPOSAL PREPARATION AND SUBMISSION INFORMATION

A. Proposal Information: Applicants are required to submit the Proposal Information prior to upload of the proposal. Complete the Proposal Information as described at https://cdmrp.org.

B. Proposal Preparation: All proposals must be converted into an electronic PDF (Portable Document Format) file for electronic proposal submission. Please see the Full Text of Program Announcement for details.

C. Submission Date and Time: Deadline: February 22, 2005. Proposals must be approved on the CDMRP eReceipt system by the Contract Representative at the applicant's institution's Sponsored Programs Office (or equivalent) by 5:00 p.m. Eastern time.

D. Electronic Submission Requirements: Electronic submission is required. No paper copy submissions will be accepted. Proposals must be submitted electronically at https://cdmrp.org. Please see the Full Text of Program Announcement for details.

VI. PROPOSAL REVIEW INFORMATION

Natural History Development Award proposals will be scientifically and programmatically reviewed by the TSCRP Integration Panel (IP), which is composed of scientific experts, clinicians, and consumer advocates. The IP will determine which proposals best fulfill the intent of the award mechanism.

VII. AWARD ADMINISTRATION INFORMATION

A. Award Notices and Administrative Requirements: Details of award notification procedures and administrative requirements including regulatory documents (Certificate of Environmental Compliance, Research Involving Human Subjects and/or Anatomical Substances, Research Involving Animals, and Safety Program Plan) can be found in the Full Text of Program Announcement.

B. Reporting Requirements: Annual reporting requirements apply.

Full Text of Program Announcement

I. GENERAL INFORMATION

A. Title of Award: Natural History Development Award (NHDA).

B. Program Name: Department of Defense (DOD) Fiscal Year 2005 (FY05) Tuberous Sclerosis Complex Research Program (TSCRP).

C. Funding Opportunity Number: TS05-NHDA.

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

E. Agency Contact(s)

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

Phone:	301-619-7079
Fax:	301-619-7792
E-mail:	cdmrp.pa@det.amedd.army.mil
Mail:	Commander US Army Medical Research and Materiel Command ATTN: MCMR-ZB-C (TS05-NHDA) 1077 Patchel Street (Building 1077) Fort Detrick, MD 21702-5024

2. Questions related to electronic submission: Help lines will be available to answer specific questions regarding the preparation of proposals for electronic submission or the process of electronic submission. The help line phone number is 301-682-5507 and is also provided on the Web. Other help desk contact information is:

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

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

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

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

H. Website to Access Application Package: Proposals must be submitted electronically at https://cdmrp.org. This website will contain all the information, forms, documents, and links needed to apply. If you experience difficulties in downloading documents, contact the CDMRP as indicated in Subsection E.2 above.

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

II. FUNDING OPPORTUNITY DESCRIPTION

A. Program History: The Natural History Development Award is part of the DOD TSCRP, which was established in FY02 to promote innovative research directed toward improved prevention, diagnosis, and/or treatment of tuberous sclerosis complex. Appropriations for the TSCRP since FY02 total $9.2 million (M). The program history of the TSCRP is shown in Table 1. The FY05 appropriation is $3.2M.

Table 1: History of the DOD's Peer Reviewed TSCRP

Program History	FY02	FY03	FY04
Congressional Appropriations for TSCRP	$1M	$2M	$3M
Total Proposals Received	13	13	40
Total Proposals Funded	3[1]	4	~12[2]
Natural History Development Award Proposals Received	N/A	N/A	1
Natural History Development Award Proposals Funded	N/A	N/A	1

[1]One FY02 proposal was partially funded with FY03 funds.
[2]Award negotiations will be finalized by September 2005.

B. Program Objectives: The overall goal of the FY05 TSCRP is to decrease the impact of tuberous sclerosis complex. Within this context, the encouragement of established scientists in the field and the attraction of new scientific expertise from other fields are essential to the tuberous sclerosis complex community. Proposals that address the needs of minority, low-income, rural, and other underrepresented and/or medically underserved populations may be submitted from any eligible institutional source. Proposals are encouraged from investigators working at Historically Black Colleges and Universities/Minority Institutions (HBCU/MI).

C. Award Mechanism Description: The intent of the Natural History Development Award is to support the development of a **focused, hypothesis-driven** natural history study that will enhance the current knowledge of TSC manifestations and improve clinical management of the disorder and/or the development and clinical testing of new interventions. **Recipients of the Natural History Development Award will be required to submit a proposal, clinical protocol, and informed consent/assent form(s) for the Natural History Study Award in FY06, pending receipt of funds by the TSCRP.**

This mechanism is **not** intended to support descriptive, broad-based proposals that are limited to collecting information (clinical, pathological, radiographical, or other) with no accompanying analysis or hypothesis testing. Instead, proposals must include a specific hypothesis or hypothesis-driven question regarding the natural history of TSC; detailed plans to develop a study to test the hypothesis or address the question; and discussion of how the proposed study will improve the clinical management of the disease and/or the design, implementation, and interpretation of clinical trials.

If the study is multi-institutional, applicants should outline in the main body of the proposal (Subsection V.F.5) the development of plans for communication and real-time data transfer among the collaborating institutions, as well as plans for handling specimens and/or imaging products obtained during the study. Participating institutions must be willing to resolve potential intellectual and material property issues and to remove institutional barriers that might interfere with achieving high levels of cooperation to ensure the successful establishment and maintenance of the consortia. An intellectual and material property plan agreed upon by all participating institutions is required as part of the administrative documentation of this proposal (see Subsection V.F.12).

Please note that all DOD-funded research involving human subjects, human anatomical substances, cadavers, and/or laboratory animals must be reviewed and approved by the USAMRMC Human Subjects Research Review Board (HSRRB) in addition to local Institutional Review Boards (IRBs). It is recommended that all protocols be prepared according to the guidelines provided in the document titled "Research Involving Human Subjects and/or Anatomical Substances," which can be found at https://cdmrp.org/Program_Announcements_and_Forms under "Regulatory Document Forms." An HSRRB-approved template for clinical protocols also can be found at this site.

All proposals for the Natural History Development Award should include:

- A statement of the **hypothesis** or the **hypothesis-driven question** that is the focus of the proposed natural history study. Applicants must articulate how the proposed study will

test the hypothesis or answer the question and describe any relevant preclinical science and preliminary clinical research that support the feasibility of the hypothesis and approaches. **Proposals must include a clearly stated hypothesis or hypothesis-driven question to be considered for funding. Proposals lacking a hypothesis or hypothesis-driven question may be administratively withdrawn;**

- The specific expected outcomes of the study as they relate to the hypothesis or question, plans to develop statistical methods to measure outcomes, and the timeframe in which the outcomes are expected to be met;
- The relevance of the proposed natural history study to TSC, including a discussion of how the results of the study will improve the clinical management of the disorder and/or facilitate the design, implementation, and interpretation of clinical trials;
- A preliminary estimate of sample size for the natural history study with appropriate statistical analyses to verify power for the sample size, a plan for generating a participant accrual/recruitment schedule, and evidence of access to appropriate participant population(s);
- A plan for the development of a clinical protocol (Manual of Operations and Procedures) and informed consent/assent form(s) that include HSRRB-prescribed content;
- The outline of a plan for obtaining internal scientific and local IRB reviews for the clinical protocol and informed consent/assent form(s) at the highest possible level within the participating institutions, up to and including preliminary IRB approval if available at your institution, by the time of the FY06 Natural History Study Award proposal submission. For multi-institutional studies, a plan for the coordination of IRB submissions must also be included;
- The outline of a plan for addressing human subjects protection requirements as outlined by the HSRRB at https://cdmrp.org/Program_Announcements_and_Forms under "Regulatory Document Forms";
- A plan for the establishment of the study team, to include names, background, qualifications, time commitments, and contributions of each team member. The study team must include:
    - A study coordinator who will guide the clinical protocol through the IRB, HSRRB, and other regulatory approval processes, coordinate activities at all participating sites, and coordinate participant accrual, and
    - A biostatistician;
- A strategy for the development and implementation of a data management plan, including:
    - A plan for the development of appropriate data collection forms,
    - A statistical plan that includes sample size calculations, methods to monitor quality and consistency of data collection, and methods to measure outcomes,
    - A plan for real-time data transfer, and
    - Data security measures;
- A preliminary study management plan, including:

    - A plan for real-time communication among collaborating institutions, if appropriate,
    - A plan for ensuring standardization of procedures across sites and among staff,
    - An organizational chart that includes a steering committee and an advisory panel consisting of scientists and consumers;
- Plans for the development of methods for the handling, distribution, analysis, banking, and security of specimens and/or imaging products. For multi-institutional studies, a specimen handling and distribution plan agreed upon by all collaborating institutions must be developed;
- A plan for public dissemination of data generated by the resulting natural history study that addresses all relevant privacy issues; and
- Evidence of preliminary institutional commitment to the proposed natural history study, including descriptions of institutional resources to be committed to the study.

The Natural History Development Award has been instituted to facilitate the funding of a quality natural history study and the rapid accrual of participants into the study through a well-developed, **HSRRB-approved** clinical protocol. The purpose of the Natural History Development Award is not to obtain preliminary data or to conduct studies to support the rationale for the proposed natural history study; therefore, **funds may not be used to support laboratory or preclinical research.** However, funds from the Natural History Development Award may be used to:

- Support meetings, teleconferences, and travel among participating investigators to develop the natural history study and associated protocol and informed consent/assent form(s);
- Furnish salary support during clinical protocol development;
- Develop and implement a data management, real-time communication, and/or administration plan for the proposed natural history study;
- Reimburse the Principal Investigator's (PI's) institution for costs associated with conducting the IRB review of the proposed clinical protocol and informed consent form;
- Provide other costs directly associated with planning and developing the natural history study;
- Coordinate informed consent/assent forms and other IRB and/or HSRRB issues between different institutions for multi-institutional studies;
- Resolve intellectual property and material rights among institutions, companies, and investigators;
- Adapt databases and other methods of data dissemination for public availability;
- Develop definitive statistical plans; and
- Develop sources and obtain letters affirming intervention supply or availability.

It is expected that the resulting natural history studies will provide resources from multiple areas such as imaging, pathology, and molecular biology, and the data set(s) generated will be useful for improved clinical management and/or meaningful evaluation of potential therapeutics for

TSC. As such, assurance of public access to all data generated by these awards and the appropriate privacy assurances regarding data transfer and distribution are required.

One requirement of the Natural History Development Award will be the submission of a proposal to the TSCRP Natural History Study Award in FY06, pending receipt of funds by the TSCRP. Another product of this award mechanism will be a detailed clinical protocol or "Manual of Operations and Procedures" for the proposed natural history study. This protocol should be in the HSRRB-approved format. Failure to submit a Natural History Study Award proposal in FY06 after receipt of an FY05 Natural History Development Award will result in a forfeit of the second installment of the FY05 Natural History Development Award funding.

Please note that the FY06 Natural History Study Award will be open to all eligible applicants with proposals relevant to the natural history of TSC. **However, there is no guarantee that funds will be available for the Natural History Study Awards in FY06.**

III. AWARD INFORMATION

Funding for the FY05 Natural History Development Award is up to $150,000 per award inclusive of both direct and indirect costs for 18 months. FY05 funds will be disbursed in two installment payments of $100,000 and $50,000 each, pending proposal, protocol, and informed consent form submission. Funds from both installments of the Natural History Development Award can cover administrative support including salary, meetings and related travel among participating investigators, database generation and software development, purchase of computers, design of websites, teleconferences, and other costs directly associated with planning and developing the natural history study. Travel costs to scientific/technical meetings may not exceed $1,800 per year per investigator. **Funds may not be used to support laboratory research.**

Disbursement of the FY05 Natural History Development Award funds will be made in two installments. The first installment of $100,000 will be made at the time of the award; the second installment of $50,000 will be made after the submission of a compliant FY06 Natural History Study Award proposal, clinical protocol, and informed consent form. **Failure to submit a Natural History Study Award in FY06 after receipt of an FY05 Natural History Development Award will result in a forfeit of the second installment of the Natural History Development Award funding.**

The nature of this Program does not allow for renewal of grants or supplementation of existing grants. Approximately $0.15M is available to the TSCRP for the Natural History Development Awards. Depending on the number and quality of the applications, it is anticipated that approximately one proposal will be funded.

IV. ELIGIBILITY INFORMATION

A. Applicants: All individuals, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by, or affiliated with, an eligible institution as defined below.

B. Institutions: Eligible institutions include for-profit, nonprofit, public, and private organizations. Examples include universities, colleges, hospitals, laboratories, companies, and agencies of local, state, and federal governments. The USAMRMC is especially interested in receiving applications from HBCU/MI.

C. Cost Sharing: It is expected that institutions will cost share. Please see full details under "Major Equipment" in Subsection V.G.2.c.

D. Other Eligibility Criteria

1. Duplicate Submissions: Submission of the same research project to the FY05 TSCRP under different award mechanisms or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative proposals.

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

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

The following will result in administrative rejection of the entire proposal prior to peer review:

- Font size is less than 12 point.
- Font type is not Times New Roman.
- Line spacing is greater than six lines per vertical inch.
- Margins are less than 0.5 inch on any side.
- Proposal body exceeds page limit.
- Proposal body is missing.

[1] Executive Orders 12876, 12900, and 13021

- Detailed cost estimate is missing.
- Proposal is incomplete after the deadline.
- Proposal does not include a hypothesis or hypothesis-driven question.

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

Unless specifically requested by the Government, any material submitted after the submission deadline will not be forwarded for peer review.

V. PROPOSAL PREPARATION AND SUBMISSION INFORMATION

A. Proposal Components Summary: This subsection is a summary of submission requirements. Details, URLs, and other links are provided in the appropriate subsections of this program announcement.

The PI is responsible for uploading the following information:

- **Proposal Information:** The Proposal Information consists of two parts, both of which are entered as data fields. A Letter of Intent is generated when Part 1 of the Proposal Information is saved.
- **Proposal Contacts:** Contact information for both the PI and the Contract Representative is required to complete the proposal submission process.
- **Statement of Work (SOW) and Proposal Abstracts:** The SOW is entered as a separate data field. The technical and public abstracts are not required for Natural History Development Award submissions, but the appropriate data fields must be completed for final submission of the proposal. Please complete these fields by entering "Not Applicable for Natural History Development Awards" in the appropriate data field(s).
- **Proposal:** The proposal is uploaded as a PDF (Portable Document Format) file under the "Required Files" tab.
- **Budget Information:** The budget information is uploaded as a PDF file under the "Required Files" tab.
- **Regulatory Documents:** The Certificate of Environmental Compliance and the Principal Investigator Safety Program Assurance form are each uploaded as separate PDF files under the "Required Files" tab.

The Contract Representative or institutional official responsible for sponsored program administration (or equivalent) from the applicant's institution is responsible for the following:

- **The Contract Representative's contact information profile must be completed prior to electronic approval of all proposal components.**
- **US Army Medical Research Acquisition Activity (USAMRAA) Required Documents:** The institution's currently negotiated "Rate Agreement," "Certifications

and Assurances for Assistance Agreements," and the "Representations for Assistance Agreements" are to be uploaded as separate PDF files under the Contract Representative's "My Profile" tab.

- **Approval:** The Contract Representative or institutional official responsible for sponsored program administration (or equivalent) must provide approval of all proposal components (Proposal Information, Proposal Contacts, SOW, Proposal, Budget Information, and regulatory documents). Contract Representative approval must occur prior to the submission deadline of 5:00 p.m. Eastern time February 22, 2005. The eReceipt system will **not** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time deadline.

B. Proposal Information: Applicants are required to submit the Proposal Information, Parts 1 and 2, prior to upload of the proposal and the budget information. Complete the Proposal Information as described in https://cdmrp.org. The Proposal Information may be "Verified & Saved" for editing purposes until "Submit Final" for approval by their Sponsored Programs Office's (or equivalent) representative.

- **Letter of Intent:** An electronic Letter of Intent should be submitted by January 25, 2005. To accomplish this, the applicant should complete Part 1 of the Proposal Information section at https://cdmrp.org, then save the information by clicking on the "Save and Forward Letter of Intent" button. This information may be changed at any time until the applicant submits the final Proposal Information by clicking on the "Submit Final" button.

C. Proposal Contacts: The Proposal Contacts **must** include the e-mail address of a representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate on behalf of the institution. The Proposal Contacts must be "Finalized" for approval by the applicant's Sponsored Programs Office's (or equivalent) representative.

D. SOW – 11,400-character limit, including spaces (approximately two pages): The SOW is captured as a data field under the "SOW/Abstract" tab in the CDMRP eReceipt system. To submit the SOW, the applicant may either type in the SOW or "cut and paste" it from a word processing application into the data field. Sample SOWs can be found at https://cdmrp.org/samples.cfm.

The SOW is a concise restatement of the research proposal that outlines, step by step, how each of the major goals or objectives of the proposed research/services will be accomplished during the timeline for which the USAMRMC will provide financial support.

As appropriate, the SOW should:

- Describe the work to be accomplished as tasks (tasks may relate to specific aims);
- Identify the timeline and milestones for the work over the period of the proposed effort;
- Indicate the number of research subjects (animal or human) projected or required for each task;

- Identify methods; and
- Identify outcomes, products, and deliverables for each phase of the project.

E. Proposal Abstracts – For the technical abstract and the public abstract, please enter "Not applicable for Natural History Development Awards." These entries are captured as separate data fields under the "SOW/Abstract" tab in the CDMRP eReceipt system and are required for final submission of your proposal.

F. Proposal

1. Format: All proposal components (proposal body, biographical sketches, publications, letters of support, etc.) must be converted into a single PDF file for electronic submission. Proposals must be uploaded under the "Required Files" tab of the CDMRP eReceipt system. Applicants unfamiliar with the preparation of PDF files are encouraged to acquire appropriate software and learn the process before the submission deadline. To prepare proposals for PDF submission, the instructions in this subsection must be followed carefully.

Please Note New Format Requirements

The proposal must be clear and legible and conform to the following guidelines:

- **Font size: 12 point or larger.**
- **Font type: Times New Roman.**
- **Spacing: Single-spaced between lines of text, no more than six lines of type within a vertical inch.**
- **Margins: Minimum of 0.5 inch in all directions.**
- **Print area: 7.5 inches x 10.0 inches (approximately 19 cm x 25.5 cm).**

Failure to adhere to the requirements for font size, font type, spacing, margins, and print area will result in administrative rejection of the entire proposal prior to peer review.

- Color, Resolution, and Multimedia Objects: Proposals may include color, high resolution, or multimedia objects (e.g., MPEG, WAV, or AVI files) embedded in the PDF files, but applicants should keep in mind that some reviewers work from black and white printed copies. Applicants may wish to include text in the proposal directing the reviewer to the electronic file for parts of the proposal that may be difficult to interpret when printed in black and white.
- Language: English.

2. Title/Referral Page: No page limit. Complete the TSCRP Title/Referral Page. Please note that all forms are available on the "Summary Tab" of eReceipt. Complete each section as described:

a. Proposal title (up to 160 characters).

b. Proposal log number (this will be automatically provided when the Proposal Information is completed and saved).

c. PI's full name (first, middle initial, last).

d. Submitting institution.

e. Award mechanism: Type in "Natural History Development Award."

f. Keyword descriptive technical terms: Please specify the subject area of the proposal. Also, list specific keywords and descriptive technical terms that would best describe the technical aspects of the project.

g. Conflicts of interest: To avoid real and apparent conflicts of interest during the review process, list the names of all scientific participants in the proposal including consultants, collaborators, and subawardees. In addition, list the names of other individuals outside the scope of this proposal that may have a conflict of interest in the review of this proposal. Provide the following information for each participant: name, institutional affiliation(s), and, if applicable, his or her role(s) on the proposed project.

3. Table of Contents/Checklist: Start section on a new page; one-page limit. Prepare a Table of Contents/Checklist, with page numbers. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Please note that headers should not be included, as the proposal log number will be electronically captured on each page of the proposal after receipt.

4. Proposal Relevance Statement: Start section on a new page; one-page limit. Applicants should state explicitly how the proposed natural history study will have a significant impact on the clinical management of TSC and/or the development and clinical testing of interventions.

5. Main Body: Start section on a new page; six-page limit inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other relevant information needed to judge the proposal. It is the responsibility of the investigator to clearly articulate how the proposed plan for a natural history study meets the intent of the mechanism. The proposal body should address the review criteria as outlined in Subsection VI.B of this program.

Describe the proposed natural history study using the following general outline:

- State the **hypothesis** or the **hypothesis-driven question** that is the focus of the proposed natural history study. Describe how the study will test the hypothesis or answer the question. State the specific expected outcomes as they relate to the hypothesis or question and the timeframe in which the outcomes are expected to be met. **Proposals must include a clearly stated hypothesis or hypothesis-driven**

question to be considered for funding. Proposals lacking a hypothesis or hypothesis-driven question may be administratively withdrawn;

- Outline the plan for the development of a clinical protocol (Manual of Operations and Procedures) and informed consent/assent form(s) that include HSRRB-prescribed content;
- Outline the plan for obtaining both internal scientific and local IRB reviews for the clinical protocol and informed consent/assent form(s) at the highest possible level within the institution, up to and including preliminary IRB approval if available at your institution, by the time of the Natural History Study Award proposal submission. For multi-institutional studies, a plan for the coordination of IRB submissions must also be included;
- Describe the development of a plan for addressing human subjects protection requirements as outlined by the HSRRB at https://cdmrp.org/Program_Announcements_and_Forms under "Regulatory Document Forms";
- Provide a description of the participant population(s), an estimated sample size for the natural history study, and a plan for generating a participant accrual/recruitment schedule. Present appropriate statistical analyses to verify power for the sample size;
- Outline the plan for the establishment of the research team, to include:
    - A study coordinator who will guide the clinical protocol through the IRB, HSRRB, and other regulatory approval processes, coordinate activities at all participating sites, and coordinate participant accrual, and
    - A biostatistician;
- Describe the strategy for the development and implementation of a data management plan, including:
    - A plan for the development of appropriate data collection forms,
    - A statistical plan that includes sample size calculations, methods to monitor quality and consistency of data collection, and methods to measure outcomes,
    - A plan for real-time data transfer, and
    - Data security measures;
- Outline the preliminary study management plan, including:
    - A plan for real-time communication among collaborating institutions, if appropriate,
    - A plan for ensuring standardization of procedures across sites and among staff, and
    - An organizational chart that includes a steering committee and an advisory panel consisting of scientists and consumers;
- Describe plans for the development of methods for the handling, distribution, analysis, banking, and security of specimens and/or imaging products. For multi-

institutional studies, a specimen handling and distribution plan agreed upon by all collaborating institutions must be developed;

- Outline the plan for public dissemination of data generated by the resulting natural history study that addresses all relevant privacy issues; and
- Provide evidence of preliminary institutional commitment to the proposed natural history study, including descriptions of institutional resources to be committed to the study. Provide a brief description of an intellectual and material property plan agreed upon by all institutions involved in the natural history study detailing how all involved are willing to resolve intellectual and material property issues.

6. Abbreviations: Start section on a new page; one-page limit. Provide a list of all acronyms, abbreviations, and symbols used.

7. 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).

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

9. Existing/Pending Support: Start section on a new page; 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. If no support exists, state "none." Proposals submitted under this program announcement should not duplicate other funded research projects.

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

11. Questionnaires, Survey Instruments, or Clinical Protocols: No page limit. Include an appropriately titled page listing the documents you have included in this section.

12. Administrative Documentation: No page limit. Submit only material specifically requested or required in this program announcement. **This section is not for additional figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, or other relevant information needed to judge the proposal.** Unrequested

material that is submitted may be construed as an attempt to gain a competitive advantage and will be removed; it may be grounds for administrative rejection of the proposal.

The first item in this section must be a list of all the items included in the Administrative Documentation section.

Provide letters of support from any collaborating individuals or institutions in this section of the proposal.

Provide letter(s) of commitment from institutions that will participate in the natural history study.

Provide documentation that institutions participating in the natural history study have an intellectual and material property plan and are willing to resolve intellectual and material property issues.

All administrative documentation must be incorporated into the electronic PDF version of your proposal. Support documentation will not be accepted separately from the electronic proposal submission. All documents or letters requiring signatures must be signed and then incorporated into the submitted proposal.

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

G. Budget Information: Budget Information includes the Detailed Cost Estimate form and Budget Justification form. Budget Information is uploaded under the "Required Files" tab of the CDMRP eReceipt system.

1. Funding Restrictions: Funding for the Natural History Development Award in FY05 is up to $150,000 per award inclusive of both direct and indirect costs for 18 months. FY05 funds will be disbursed in two installment payments, pending proposal, clinical protocol, and informed consent form submission. Funds from both installments of the Natural History Development Award can cover administrative support including salary, meetings and related travel among participating investigators, database generation and software development, purchase of computers, design of websites, teleconferences, and other costs directly associated with planning and developing the natural history study. Travel costs to scientific/technical meetings may not exceed $1,800 per year per investigator. **Funds may not be used to support laboratory research.**

Please note that there is no guarantee that funds will be available for the subsequent Natural History Study Awards in FY06.

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

to use discretion in budget requests. Budgets also will be reviewed during award negotiations. **Organizations must provide sufficient detail and budget justification so that the Government can determine the proposed costs to be allocable and reasonable for the proposed research.** The Detailed Cost Estimate form and Budget Justification for your proposal must be uploaded as a PDF file, separate from the proposal.

Costs proposed must conform to the following regulations and principles:

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

The following section provides instructions for preparing the Detailed Cost Estimate form. All amounts entered should be in U.S. dollars.

a. Personnel

i. Name: Starting with the PI, list the names of all participants who will be involved in the project during the initial budget period, regardless of whether salaries are requested. Include all collaborating investigators, research associates, individuals in training, and support staff. Only **ONE** person may be identified as the PI of the proposal.

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

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

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

v. Percentage of Effort on Project: The qualifications of the PI and the amount of time that he or she and other professional personnel will devote to the research are important factors in selecting research proposals for funding. For each key staff member identified on the budget form, list the percentage of each appointment to be spent on this project.

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

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

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

b. Consultant Costs: Regardless of whether funds are requested, provide the names and organizational affiliations of all consultants.

c. Major Equipment: It is the policy of the DOD that all commercial and nonprofit recipients provide the equipment needed to support proposed research. In those rare cases in which specific additional equipment is approved for commercial and nonprofit organizations, such approved cost elements shall be separately negotiated. Moreover, it is expected that institutions will share 50% of the cost of equipment purchased for this research proposal when individual equipment costs are equal to or exceed $5,000.

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

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

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

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

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

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

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

j. Total Costs for the Entire Proposed Period of Support (second page of the Detailed Cost Estimate form): Enter the totals under each budget category for all additional years of support requested and itemize these totals in the Budget Justification section of the Detailed Cost Estimate form. Note with an asterisk (*) and explain any significant increases or decreases from the initial year budget. All amounts should be in U.S. dollars. Total costs for the entire proposed period of support should equal the amount previously entered online in the Proposal Information https://cdmrp.org.

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

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

Do not submit other regulatory documents (Research Involving Human Subjects and/or Anatomical Substances/Cadavers; Research Involving Animals) with the proposal. Instead, the applicant should provide these documents to the USAMRMC only upon request.

I. USAMRAA Required Documents: The most current version of the institution's negotiated "Rate Agreement," the "Certifications and Assurances for Assistance Agreements", and the "Representations for Assistance Agreements" must be uploaded by the Contract Representative from the Sponsored Programs Office (or equivalent). These documents must be uploaded as separate PDF files under the Contract Representative's "My Profile" tab of the CDMRP eReceipt system prior to negotiations.

J. Submission Date and Time: Proposals must be approved on the CDMRP eReceipt system by the Contract Representative at the applicant's institution's Sponsored Programs Office (or equivalent) by the deadline. If your proposal is either incomplete or not approved electronically before the deadline, it will not be considered for review. The eReceipt system will **not** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time February 22, 2005 deadline.

The timeline for the Natural History Development Award is:

Online Letter of Intent:	Expected by **January 25, 2005**
Online Proposal Information:	Prior to proposal submission
Proposal Submission/Approval Deadline:	**5:00 p.m. Eastern time February 22, 2005**
Proposal Review:	March 2005
Request for Additional Documents:	As early as 2 weeks after the completion of proposal review
Notification Letter:	Approximately 4 weeks after proposal review
Award Start Date:	**As early as May 2005**

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

Several steps are critical to successful proposal submission:

- The Proposal Information must be submitted prior to submission of the proposal. Applicants are encouraged to begin this part of the submission process early.
- Proposal Contacts must be submitted prior to submission of the proposal. The e-mail address of a Contract Representative from the Sponsored Programs Office (or equivalent) must be included in the Proposal Contacts. Applicants are encouraged to begin this part of the submission process early.
- Applicants are encouraged to coordinate early with their Sponsored Programs Office (or equivalent).
- The Contract Representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate on behalf of the institution is required to provide final approval before the proposal is accepted.

- The eReceipt system will **not** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time February 22, 2005 deadline.
- Any supporting documentation that the applicant includes with the proposal must be incorporated into the PDF file prior to upload.
- Some items to be included in the proposal will need to be scanned. These items might include figures, tables, letters, or publications. All scanned documents, including figures, tables, and graphs, should be scanned at a resolution of 300-400 dpi or less.
- Budget Information includes the Detailed Cost Estimate form and the Budget Justification form. Budget Information must be uploaded under the "Required Files" tab of the CDMRP eReceipt system.
- The regulatory documents required at submission include a completed, signed Certificate of Environmental Compliance and a completed, signed Principal Investigator Safety Program Assurance form. These must be uploaded under the "Required Files" tab of the CDMRP eReceipt system.

VI. PROPOSAL REVIEW INFORMATION

A. Proposal Review and Selection Overview: Natural History Development Award proposals will be scientifically and programmatically reviewed by the TSCRP Integration Panel (IP), which is composed of scientific experts, clinicians, and consumer advocates. The IP will determine which proposals best fulfill the intent of the award mechanism.

B. Review Criteria: Natural History Development Award proposals will be evaluated according to the following criteria:

- **Hypothesis:** Does the applicant provide a clear and focused hypothesis or hypothesis-driven question that will drive the proposed natural history study? Does the applicant convincingly demonstrate that the proposed study will test the hypothesis or answer the question? Does the applicant describe the specific expected outcomes of the study as they relate to the hypothesis or question, the development of statistical methods to measure outcomes, and the timeframe in which the outcomes are expected to be met?
- **Clinical Relevance:** Do existing preclinical and/or preliminary clinical data support the relevance of the natural history study to TSC? Does the proposed study address an important clinical and/or diagnostic problem, and is it likely to have a substantial impact on the clinical management of the disease and/or the design, implementation, and interpretation of clinical trials?
- **Natural History Study:** Are the plans for the development of a natural history study, clinical protocol, and informed consent/assent form(s) within the performance period appropriate? Is there a plan for obtaining regulatory approval(s) for the protocol and informed consent/assent form(s) at the highest possible level within the institution, up to and including preliminary IRB approval, by the time of the Natural History Study Award proposal submission? Is there a plan for addressing human subjects protection requirements as described by the HSRRB? Are the preliminary sample sizes and

participant accrual plans reasonable? Is there a strategy for the development and implementation of a data management plan, including a clear statistical plan? Is there an outline of an appropriate study management plan? Are there plans for the development of specimen handling, distribution, and banking methods? Are there plans to make all data generated by the proposed natural history study publicly available, and have all privacy issues associated with public availability been addressed?

- **PI and Personnel:** Does the PI have expertise in TSC? Are the PI and other key personnel appropriately trained and well suited to carry out this work? Is there representation from all the areas of expertise needed to conduct the natural history study successfully?
- **Institutional Commitment:** Is there evidence of institutional commitment to the proposed natural history study at each participating institution? Is there evidence of an intellectual and material property management plan that is agreed upon by all participating institutions?

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

VII. AWARD ADMINISTRATION INFORMATION

A. Award Notices: After the evaluation process is completed, every applicant will receive notification of the award status of his or her proposal. Applicants can expect to be notified of the agency's decision in April 2005.

B. Administrative Requirements: All awards are made to organizations, not individuals. A PI should submit a proposal through, and be employed by or affiliated with, a university, college, non-profit research institution, commercial firm, or government agency (including military laboratories) to receive support. To be eligible for an 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 (OMB Circular A-110 and DOD Grant and Agreement Regulations). *Any organization requesting receipt of an award from this announcement must be registered in the Central Contractor Registration (CCR) database. Access to the CCR online registration is through the CCR homepage at http://www.ccr.gov/*

Any change in the institution, the PI, and/or the SOW will require that the PI resubmit contact information. Any delay in the submission of updated information could result in a delay in the contracting and regulatory review and a subsequent delay in payment.

C. Award Negotiation: Award negotiation consists of discussions, reviews, and justifications of critical issues involving the USAMRAA. A Contract Specialist and/or representative from the USAMRAA will contact the Contract Representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate contracts and grants at the applicant's institution. As

part of the negotiation process, additional documentation and justifications related to the proposed SOW and associated budgets may be required.

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

D. Regulatory Review

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

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

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

A Facility Safety Plan is also required and will be requested at a later date. However, your institution may already have an approved Facility Safety Plan. To determine the status of approval, check the USAMRMC website at https://mrmc.detrick.army.mil/crprcqsohdfsplan.asp. If your institution is not listed on the aforementioned website, contact your Facility Safety Director/Manager to initiate completion of the institution-based Facility Safety Plan. Specific requirements for the Safety Program Plan can be found at https://mrmc.detrick.army.mil/docs/rcq/FY02FSPAppendix.doc.

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

4. Research Involving Animal Use: Animal use documents should not be submitted with the proposal and will be requested at a later date. Specific requirements for research involving animals can be found at https://mrmc.detrick.army.mil/docs/rcq/FY05AnimalAppendix.doc.

5. Research Involving Human Subjects/Anatomical Substances/Cadavers: (See Subsection V.H for information pertaining to the submission of human subjects and/or human anatomical substances documents or cadavers.) In addition to local IRB approval to conduct research involving human subjects and/or anatomical substances or cadavers, a second tier of IRB review and approval is also required by the DOD. This second review is conducted by the HSRRB, which is administered by the USAMRMC Office of Research

Protections (ORP) (formerly Regulatory Compliance and Quality). The HSRRB is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous and detailed and will require information in addition to that supplied to the local review board. For example:

- Intent to Benefit. In the development of a research protocol for submission to the DOD, the applicant must specifically address, if applicable, the Intent to Benefit. An individual not legally competent to consent (e.g., minors) may not be enrolled in DOD-sponsored research unless the research is intended to benefit each and every subject enrolled in the study. Applicants should be aware that this law makes placebo-controlled clinical trials problematic because of the 'intent to benefit' requirement whenever participation is sought of subjects from whom consent must be obtained by the legally authorized representative.
- The DOD considers cell lines of human origin to be human anatomical substances/cadavers. Use of these cell lines is subject to HSRRB review and approval.

Specific requirements for research involving human subjects, human anatomical substances, and/or cadavers can be found at https://mrmc.detrick.army.mil/docs/rcq/HumanSubjectsAppendix(13May04).doc. An informed consent form template can be located at https://mrmc.detrick.army.mil/docs/rcq/Proconsent/ConsentFormGuidelines.doc.

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

E. Reporting: All research awards will require the timely delivery of several reports during the research effort.

- **Research Progress Report Requirements:** Reporting requirements consist of an annual report (for each year of research except the final year) that presents a detailed summary of scientific issues and accomplishments and a final report (submitted in the last year of the award period) that details the findings and issues for the entire project.

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

VIII. OTHER INFORMATION

A. Disclosure of Proprietary Information outside the Government: By submission of a

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

B. Government Obligation: Applicants are cautioned that only an appointed Contracting/Grants Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government to fund preparation of a proposal or to support research should be inferred from discussions with a technical project officer. Applicants who, or organizations that, make financial or other commitments for a research effort in the absence of an actual legal obligation signed by the USAMRAA Contracting/Grants Officer do so at their own risk.

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

D. 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 CDMRP staff, the USAMRMC Judge Advocate General staff, and the USAMRAA Grants Officers constitute an Inquiry Review Panel and review each inquiry to determine whether factual or procedural errors in either peer or programmatic review have occurred, and if so, what action should be taken.

E. Title to Inventions and Patents: In accordance with the Bayh-Dole Act (35 USC 200 et seq.[2]), title to inventions and patents resulting from such federally funded research may be held by the grantee or its collaborator, but the U.S. Government shall, at a minimum, retain nonexclusive rights for the use of such inventions. An investigator must follow the instructions in the assistance agreement concerning license agreements and patents.

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

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

IX. ACRONYM LIST

AVI	Audio Video Interleave
CCR	Central Contractor Registration
CDMRP	Congressionally Directed Medical Research Programs
CFDA	Catalog of Federal Domestic Assistance
DOD	Department of Defense
FY	Fiscal Year
HBCU/MI	Historically Black Colleges and Universities/Minority Institutions
HSRRB	Human Subjects Research Review Board
IP	Integration Panel
IRB	Institutional Review Board
M	Million
MPEG	Moving Picture Experts Group
NHDA	Natural History Development Award
OMB	Office of Management and Budget
ORP	Office of Research Protections (formerly Regulatory Compliance and Quality)
PDF	Portable Document Format
PI	Principal Investigator
SOW	Statement of Work
TSCRP	Tuberous Sclerosis Complex Research Program
USAMRAA	US Army Medical Research Acquisition Activity
USAMRMC	US Army Medical Research and Materiel Command
USC	United States Code
WAV	Wave