



Funding Research ■ Changing Practice ■ Creating Awareness

Research Guidelines

Introduction

The funding for this round of NTI awards is administered through the Department of Defense (DOD), and therefore, there are specific requirements and human subjects compliance review procedures that must be adhered to. This guide will provide a reference and explanation of the various requirements for both NTI and DOD.

The following sections are included in this document:

- A. Introduction to DOD Agencies
- B. Levels of Review
- C. Patient Consent
- D. Protocol
- E. Protocol-Related Reporting Requirements
- F. Documentation required by NTI or HRPO
- G. Reports and Publications

A. DOD AGENCIES THAT MAY BE INVOLVED IN THE HUMAN SUBJECTS COMPLIANCE REVIEW OF YOUR SUBAWARD:

1. The U.S. Army Medical Research and Materiel Command (USAMRMC)
 - o This agency manages and provides oversight for all DOD funded biomedical research.
2. The Human Research Protection Office (HRPO) of the DOD/USAMRMC
 - o This office provides oversight and second level review of human research. This Second Level review is required by the DOD.
3. The Commanding General's Research Advisory Board, the Human Subjects Research Review Board (HSRRB)

Please note that NO research can be started without approval notification from NTI and USAMRMC. There will be NO reimbursement for any research conducted prior to approval from NTI and USAMRMC. Studies that are started without prior consent will be subject to cancellation.

NTI will submit the research protocol and all supporting documents to USAMRMC/HRPO on your behalf and assist in the approval process. The HRPO approval process generally takes 6-8 weeks to complete. The Principal Investigator will receive approval notification via e-mail from HRPO and NTI. Notification of approval from HRPO and NTI must be obtained before clinical work may begin. The following highlight specific requirements unique to DOD/USAMRMC supported research that must be included either in the consent or the protocol.

B. LEVELS OF REVIEW

Level 1: IRB of record approval

Level 2: Human Research Protection Office (HRPO) of the DOD/USAMRMC

Level 3: (if applicable) Human Subjects Research Review Board (HSRRB)

Studies meeting the following specific criteria will be reviewed by the HSRRB:

- “First in humans” INDs, devices, biologics, and vaccines
- Gene transfer studies
- Studies involving non-lethal weapons
- INDs with high toxicity profiles
- Issues regarding non-compliance with human subjects protection regulations
- Protocols determined by the Deputy, ORP and/or ORP HRPO designee(s) to require HSRRB review (e.g., protocols involving complex regulatory/ethical issues, protocols requiring Secretary of the Army waiver)

Studies not meeting these criteria will not require HSRRB review. For studies requiring HSRRB review, the assigned DOD Human Subjects Protection Scientist (HSPS) will inform the Investigators of this requirement and assist them with preparing for, scheduling and coordinating attendance at the Board meeting to address Board member questions via an audio link.

C. PATIENT CONSENT:

The following must appear in the consent form:

1. A statement that the DOD is funding the study.
2. A statement that representatives of the USAMRMC or the DOD are authorized to review research records.
3. In the HIPAA authorization section, representatives of the USAMRMC must be listed as one of the parties to whom private health information may be disclosed.

D. PROTOCOL:

When applicable, the following DOD unique requirement must be addressed in the protocol prior to USAMRMC approval:

10 United States Code 980. The requirements of Title 10 United States Code 980, which are applicable to DOD sponsored research, must be considered. 10 USC 980 requires that “Funds appropriated to the Department of Defense may not be used for research involving a human being as an experimental subject unless:

- (1) the informed consent of the subject is obtained in advance; or
- (2) in the case of research intended to be beneficial to the subject, the informed consent may be obtained from a legal representative of the subject.”

Furthermore, and consistent with the Common Federal Policy for the Protection of Human Subjects, if an individual cannot give his or her own consent to participate in a research study,

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

Note: This statute is only applicable to certain intervention studies. 10 USC 980 does not apply to retrospective studies, observational studies, blood draws and tissue collections. Contact Kim Overton (kim.overton@nationaltraumainstitute.org or (210) 233-6162 x 210) for further clarifications regarding applicability of 10 USC 980 to your specific protocol.

Medical Monitor Requirement:

For all greater than minimal risk protocols, an independent medical monitor must be identified in the protocol. The role of the medical monitor must be described in the risk/benefit section of the protocol and be consistent with DOD guidance. The medical monitor must have no real or apparent conflict of interest and should not be under the supervision of the principal investigator or other investigators or research staff. Medical monitors should be physicians, dentists, psychologists, nurses, or other healthcare providers capable of overseeing the progress of research protocols, especially issues of individual volunteer management and safety. Medical monitors must be independent of the investigative team and possess sufficient educational and professional experience to serve as the volunteer advocate. Depending on the nature of the study, the medical monitor may be assigned to assess one or more of the following phases of research project: volunteer recruitment, volunteer enrollment, data collection, or data storage and analysis. The medical monitor will provide an independent evaluation of serious adverse events and unanticipated problems involving risk to subjects or others to the IRB, NTI and the HRPO. The medical monitor may be assigned to discuss research progress with the principal investigator, interview volunteers, consult on individual cases, or evaluate adverse event reports. Medical monitors shall promptly report discrepancies or problems to the IRB, NTI and the HRPO. They shall have the authority to stop a research study in progress, remove individual volunteers from a study, and take whatever steps are necessary to protect the safety and well-being of research volunteers until the IRB can assess the medical monitor's report. It is acceptable to provide appropriate compensation to the medical monitor for his or her services.

Military Personnel as Research Subjects:

Recruitment of Military Personnel: Civilian investigators attempting to access military volunteer pools are advised to seek collaboration with a military investigator who will be familiar with service-specific requirements. A letter of support from the Commander of military facilities or units in which recruitment will occur, or the study will be conducted, will be requested by the HRPO. Some military sites may also require that each volunteer seek written permission from their supervisor prior to participation in research studies. Special consideration must be given to the recruitment process for military personnel. The Chain of Command must not be involved in the recruitment of military personnel and cannot encourage or order service members to participate in a research study. Per DOD Directive 3216.02, an ombudsman must be employed when conducting group briefings with Active Duty personnel to ensure that volunteers understand that participation is voluntary and may be recommended in other situations as well, especially when young enlisted service members are recruited who are trained to follow orders. Service members are trained to act as a unit, so peer pressure should also be considered and minimized if possible.

Payment to 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 volunteers may not receive any other payment for participation in a research study unless they are off duty or on leave during the time they are participating in the protocol.

Confidentiality for Military Personnel: Confidentiality risk assessment for military personnel requires serious consideration of the potential to affect the military career. Medical and psychological diagnoses can lead to limitation of duties or discharge. Information regarding alcohol or drug abuse, drunk driving, sexual or spousal abuse and sexual orientation can lead to actions under the Uniform Code of Military Justice (UCMJ) including incarceration and dishonorable discharge. For aviators, losing flight status due to a physical or psychological concern is an issue.

Protocol Specifics:

The USAMRMC will review your protocol for the following specific information, please ensure you have described these items.

1. **Type of study proposed:** i.e., Phase I trial, pilot study, laboratory experiment, intervention, survey/record review, longitudinal, retrospective, etc.
2. **Procedures to be performed:** Administration of experimental drug, collection of biological specimens, diagnostic procedures, procedures involving radiation or radioactive materials, etc.
3. **Drug(s) to be used and type**
4. **Subject Information:** age range, gender, total number of patients to be enrolled by site.
5. **Consent information:** will subjects be able to provide their own consent, will Legal Authorized Representative consent be obtained prior to enrollment, description of intent to benefit each subject, any actions taken as a result of research related findings.

E. PROTOCOL-RELATED REPORTING REQUIREMENTS:

The following are reporting requirements and responsibilities of the Principal Investigator to NTI. Failure to comply could result in suspension of funding:

1. Major modifications to the research protocol and any modifications that could potentially increase risk to subjects must be submitted to NTI for HRPO approval prior to implementation. Major modifications include a change in Principal Investigator, change or addition of an institution, elimination or alteration of the consent process, change in age range, or change in/addition to the study population, and changes that could potentially increase risk to subjects.
2. All unanticipated problems involving risk to subjects or others, serious adverse events related to participation in the study and related subject deaths must be promptly reported by phone to Kim Overton at NTI (210) 233-6162 x 210. Further reports will be required, as instructed by Ms. Overton for HRPO compliance.
3. Suspensions, clinical holds (voluntary or involuntary), or terminations of this research by the IRB, the institution, the Sponsor, or regulatory agencies will be promptly reported to NTI.
4. Any deviation to the protocol that may have an adverse effect on the safety or rights of the subject or the integrity of the study must be reported to NTI as soon as the deviation is identified.
5. The PI will receive email notification from HRPO and NTI regarding the continuing review. A copy of the continuing review report and re-approval notification by the IRB of Record must be submitted to NTI as soon as possible after receipt of approval. Please note that the HRPO also conducts random audits at the time of continuing review and additional information and documentation may be requested at that time.
6. The final study report, including a copy of any acknowledgement documentation and any supporting documents, must be submitted to NTI as soon as all documents become available. The PI will receive closeout notification from HRPO and NTI.
7. The knowledge of any pending compliance inspection/visit by the FDA, OHRP, or other government agency concerning this research, the issuance of Inspection Reports, FDA Form 483, warning letters or actions taken by any regulatory agencies including legal or medical actions and any instances of serious or continuing noncompliance with the regulations or requirements must be reported immediately to NTI.

Please Note: The USAMRMC-ORP-HRPO conducts random site visits as part of its responsibility for compliance oversight. Accurate and complete study records must be maintained and made available to representatives of the USAMRMC as a part of their responsibility to protect human subjects in research. Research records must be stored in a confidential manner so as to protect the confidentiality of subject information.

F. DOCUMENTATION REQUIRED BY NTI OR HRPO:

This documentation is required for the USAMRMC approval process. Please submit this documentation to Kim Overton (kim.overton@nationaltraumainstitute.org) as a complete package of documentation.

1. IRB-approved Research Protocol
2. Site-specific Consent/Assent/HIPAA Authorization Form(s)
3. *Curriculum Vitae* or Biosketch for Principal Investigator, Medical Monitor and Key Research Personnel at each site
4. Documentation of human subjects protection training (within last three years) for the Principal Investigator (PI) and all Associate Investigators (AI)
5. Letter from the IRB with the following information: (a) protocol risk level from IRB (exempt, NGTMR, GTMR); (b) date of IRB approval; (c) next continuing review date; (d) any waivers approved; and (e) risk for medical devices (non-significant risk or significant risk)
6. Site-Specific Recruitment Materials, e.g., advertisements, posters, and announcements, recruitment letters, phone scripts, briefing materials
7. Study Instruments (e.g. questionnaires, interview guides, etc.), case report form(s), data collection/recording form(s)
8. Additional Committee and Regulatory Approvals, e.g., Radiation Control Committee, Institutional Biosafety Committee, RAC review, FDA letters
9. Samples of Other Documents to be Signed by the Subject, e.g., Procedural Consent Forms, Sample Donation Forms, Consent for Testing or Communicable Diseases, Photo Release Form, Future Contact Form
10. Federal wide or DOD Assurance Number for awardee and each research site
11. IRB Approval Letter from an IRB listed on assurance for awardee and each research site (or appropriate IRB authorization agreement)
12. Site-Specific Protocol Addendum describing site specific implementation of the protocol (including, but not limited to, recruitment, informed consent, differences in research procedures, optional procedures, handling and transport of specimens and data, site reporting requirements). A description of any unique aspects to the study population at the site should be included (for example, low socioeconomic status, non-English speaking, cultural or religious beliefs, illegal immigrants, etc.).
13. Conflict of Interest Forms for Key Research Personnel at each site
14. Additional Requirements for IND or Device Protocols:
 - a. Document specifying IND/IDE Number
 - b. Investigator's Brochure or Manufacturer's Device Manual/device information
 - c. A signed Form FDA 1572
 - d. Document from manufacturer declaring level of risk for device (non-significant risk or significant risk) and IDE form
 - e. Documentation of the Investigator's most recent GCP training (if available)
 - f. Completed PI Assurance document

G. REPORTS AND PUBLICATIONS:

1. **Reports:** Once the subaward is executed, the PI will receive an email regarding the schedule of quarterly, annual, and final reports. The PI will also receive periodic reminders prior to report due dates. The quarterly report template is

attached as Appendix A. The annual/final report components are included in the subaward contract.

2. **Publications/Presentations:** Copies of any publications, presentations, or manuscripts resulting from these studies should be sent to NTI immediately upon availability and with the quarterly, annual, and final reports.
3. **Publication acknowledgement:** The following publication acknowledgement is required on all publications:

“This work was funded by NTI Subaward # [refer to your subaward agreement] from the National Trauma Institute and sponsored by the Department of the Army, Prime award # [refer to your subaward agreement]). The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD 21702-5014 is the awarding and administering acquisition office. The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.”

For any questions/concerns/issues, please contact:

Kim Overton

Research Coordinator

kim.overton@nationaltraumainstitute.org

Phone: (210) 233-6162 x 210.

APPENDIX A: QUARTERLY REPORT TEMPLATE

NATIONAL TRAUMA INSTITUTE QUARTERLY REPORT

Subaward No:		Report Date:	
Reporting Period:		PI Name:	
Telephone No:		Institution:	
Project Title:			

SCIENTIFIC PROGRESS [Describe scientific progress for the quarter in terms of the tasks or objectives listed in the statement of work for this subaward]

STATEMENT OF PLANS FOR NEXT QUARTER [Present a statement of plans or milestones for the next quarter.]

Name of Preparer

Signature of Preparer:
