RESEARCH SUPPORTED BY A
DEPARTMENT OF DEFENSE (DOD) COMPONENT

2/19/2016

The following special considerations apply to research involving human subjects supported by a DoD Component through a contract, grant, cooperative agreement, or other arrangement. Research is considered to involve the DoD if it is conducted in collaboration with DoD employees, uses DoD facilities, or will intentionally include DoD personnel as experimental subjects. Any institution engaging in research that involves the DoD must possess a valid Federal Wide Assurance (FWA).

Department of Defense components include, but may not be limited to:

- Department of Defense
- Navy
- Office of Naval Research
- Naval Academy
- U.S. Naval Observatory
- Army
- U.S. Army Corps of Engineers
- Military Academy (West Point)
- Air Force
- Air Force Academy
- Marines
- Coast Guard
- National Guard
- Missile Defense Agency
- Defense Advanced Research Projects Agency (DARPA)
- Pentagon Force Protection Agency
- Defense Intelligence Agency
- National Geospatial-Intelligence Agency
- National Security Agency
- National War College

Research funded by the DoD shall have a DoD assurance of compliance. Investigators of DoD-funded research must contact the IRB Executive Director to initiate the procedure for obtaining a DoD assurance.

Research supported by the DoD that affects vulnerable classes of subjects shall meet the additional protections of 45 CFR 46, Subparts B, C, and D, as applicable.

Prisoners of War
The involvement of prisoners of war as human subjects of research is prohibited. A prisoner of war is any person captured, detained, held, or otherwise under the control of Department of Defense (DoD) personnel (military and civilian, or contractor employee) except DoD personnel held for law enforcement purposes.

Experimental Subject
An experimental subject is a human being involved in an activity for research purposes, where there is an intervention or interaction for the primary purpose of obtaining data regarding the effect of the intervention or interaction (32 CFR 219.102 (f)). Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject’s environment, or the withholding of an intervention that would otherwise have been undertaken if not for the research purpose.

**Prior Informed Consent**

In general, no DoD Component may conduct or use appropriated funds to support research involving a human being as an experimental subject without the prior informed consent of the subject, unless a waiver of consent is approved by the Head of a DoD Component (see below).

In the case of research intended to be beneficial to the subject, if the subject lacks capacity, due to age, condition, or other reason, to make a legally effective decision regarding consent to participate in the research, prior consent may be provided by a legal representative of the subject. The determination that the research is intended to be beneficial to the subject must be made by an Institutional Review Board (IRB). If consent is to be obtained from the experimental subjects’ legal representative, the research must intend to benefit the individual subject.

If the research subject meets the definition of “experimental subject,” policies and procedure prohibit a waiver of the consent process unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering. The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met:

- The research is necessary to advance the development of a medical product for the Military Services.
- The research may directly benefit the individual experimental subject.
- The research is conducted in compliance with all other applicable laws and regulations.
- For classified research, waivers of consent are prohibited.

If the research subject does not meet the definition of “experimental subject,” policies and procedures allow the IRB to waive the consent process.

An exception from consent in emergency medicine research (sometimes referred to as planned emergency research) is prohibited unless a waiver is obtained from the Secretary of Defense.

**Research Monitor**

For research involving more than minimal risk (as defined in 32 CFR 219.102(i)) to subjects, an independent research monitor shall be appointed by name. The IRB or institutional official can require this for a portion of the research or for studies involving no more than minimal risk, if appropriate. There may be more than one research monitor.
(e.g., if different skills or experience are needed). The research monitor shall be independent of the team conducting the research.

Research monitors shall be physicians, dentists, psychologists, nurses, or other healthcare professionals capable of overseeing the progress of research protocols, especially issues of individual subject/patient management and safety. The monitor may be an ombudsman or a member of the data safety monitoring board. Research monitors shall possess sufficient educational and professional experience to serve as the subject/patient advocate. The IRB must approve a written summary of the monitors’ duties, authorities, and responsibilities.

The IRB or institutional official shall communicate with research monitors to confirm their duties, authorities, and responsibilities. Depending on the nature of the study, the research monitor may be assigned to assess or observe one or more of the following phases of a research project: subject recruitment, subject enrollment procedures, the consent process, study interventions and interactions, data collection, or data storage and analysis, and to review monitoring plans and unanticipated problems involving risks to subjects or others. At the discretion of the IRB, the research monitor may be assigned to discuss research progress with the principal investigator, interview subjects, or consult with others outside of the study. Research monitors shall promptly report discrepancies or problems to the IRB. They shall have the authority to stop a research study in progress, remove individual subjects from a study, and take whatever steps are necessary to protect the safety and well-being of research subjects until the IRB or the institutional official can assess the problem.

Requirement to Minimize Undue Influence
Additional protections for military research subjects to minimize undue influence must be present. For research involving more than minimal risk and also involving military personnel, unit officers and noncommissioned officers (NCOs) shall not influence the decisions of their subordinates to participate or not to participate as research subjects. Unit officers and senior NCOs in the chain of command shall not be present at the time of research subject solicitation and consent during any research recruitment sessions in which members of units under their command are afforded the opportunity to participate as research subjects. When applicable, officers and NCOs so excluded shall be afforded the opportunity to participate as research subjects in a separate recruitment session. During recruitment briefings to a unit where a percentage of the unit is being recruited to participate as a group, an ombudsman not connected in any way with the proposed research or the unit shall be present to monitor that the voluntary nature of individual participants is adequately stressed and that the information provided about the research is adequate and accurate.

Conflict of Interest
Conflict of interest can be defined as any situation in which financial or personal interests may compromise or present the appearance of compromising an individual’s or group’s judgment in conducting, reviewing, approving, managing, and supporting research. Investigators, key research personnel, IRB members, and other personnel must
disclose all conflicts of interest, including any financial interests for themselves, spouses, and dependent children. No person shall be involved in any review or approval of a protocol when there may be a conflict of interest.

**Noncompliance or Research Misconduct**

Any determinations of serious or continuing non-compliance of DoD supported research must be promptly reported to the DoD human research protection officer. Records maintained that document compliance or non-compliance with DoD regulations shall be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

For additional requirements regarding Department of Navy (DoN)-sponsored research, see below.

Addressing and reporting allegations of research misconduct shall occur. The DoD Components that conduct or support research shall ensure that data and data collection are conducted in an ethical manner. In cases in which data are not collected in an appropriate manner, the DoD Component shall determine if the misconduct was intentional or reckless; was an isolated event or part of a pattern; had significant impact on the research record; or had significant impact on other researchers or institutions. The DoD Component shall initiate and carry through on any actions that are necessary to ensure resolution of misconduct findings.

**Research Involving Vulnerable Populations**

Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C. and D.

- For purposes of applying Subpart B, the phrase “biomedical knowledge” shall be replaced with “generalizable knowledge.”
- The applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.
- Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.
- Research involving prisoners cannot be reviewed by the expedited procedure.
- When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.
- In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:
  - The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.
  - The research presents no more than minimal risk.
  - The research presents no more than an inconvenience to the subject.
  - When a prisoner becomes a subject, if the researcher asserts to the IRB that it is in the best interest of the prisoner-subject to continue to participate in the
research while a prisoner, the IRB chair may determine that the prisoner-subject may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the institutional official and DoD Component office review the IRB’s approval to change the research protocol. Otherwise, the IRB chair shall require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol. The convened IRB, upon receipt of notification that a previously enrolled human subject has become a prisoner, shall promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner-subject can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-subject’s confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human participants from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-subject to continue to participate in the research. This approval is limited to the individual prisoner-subject and does not allow recruitment of prisoners as participants.

- Research involving a detainee as a human participants is prohibited.
- This prohibition does apply to research involving investigational drugs and devices when the same products would be offered to US military personnel in the same location for the same condition.
- The exemption for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.
- Policies and procedures prohibit research involving prisoners of war.
- The IRB is aware of the definition of “prisoner of war” for the DoD component granting the addendum.

**Additional Requirements for Research Funded by a DoD Component**

1.) New research protocols and substantive amendments to approved research must undergo scientific approval prior to or concurrent with IRB review. Substantive amendments are those that involve more than minimal risk and thus require full board review. For non-exempt research, the IRB must consider the scientific merit of the research. The IRB may rely on outside experts to provide an evaluation of the scientific merit.

2.) For all personnel who conduct, review, approve, oversee, support, or manage human subject research, initial and continuing research ethics education will occur as described in the DUHS HRPP policy titled “Required Education on Protection of Human Subjects”. For research supported by a DoD component, the IRB staff, IRB
Chair and members, and the investigator(s) and research staff become aware of the specific requirements contained in the DoD regulations and requirements and are educated about these requirements by reviewing this policy and completing the requisite online training specific to DoD requirements. The DoD component may evaluate the education policies of the DUHS HRPP to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.

3.) Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD after the research protocol is reviewed and approved by the IRB.

4.) For any DoD-supported researcher, the following shall be promptly reported to the DoD human research protection officer:

- When significant changes to the research protocol are approved by the IRB.
- The results of the IRB continuing review.
- Change of reviewing IRB.
- When the organization is notified by any Federal department, agency or national organization that any part of an HRPP is under investigation for cause involving a DoD-supported research protocol.

5.) Every project involving greater than minimal risk shall include an arrangement for emergency treatment and necessary follow-up of any research-related injuries. The IRB will determine whether research involving minimal risk also might include a similar arrangement for research-related injury. DUHS IRB’s standard language for research-related injury will be used. Added information may be included if required by the DoD component.

6.) Additional safeguards for research conducted with international populations must be provided. Research involving human subjects who are not U.S. citizens or DoD personnel, conducted outside the United States, its territories and possessions, requires permission of the host country as evidenced by certification from the host country or local ethics review. The local laws, regulations, customs, and practices of the host country will be followed.

7.) Limitations on compensation for U. S. military personnel must exist. Dual compensation must not occur, such that an individual must not receive pay or compensation for research occurring during duty hours. However, US military personnel may be compensated for research if the subject is involved in the research when not on duty.

8.) Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw. Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.
9.) Recordkeeping requirements include maintaining adequate documentation of DoD-supported or -conducted research involving human subjects and establishing procedures for supporting DoD reporting requirements.

10.) All research involving the use of investigational test articles (drugs, devices and biologics) shall comply with U.S. Food and Drug Administration (FDA) regulations. An Investigational New Drug (IND) application or an Investigational Device Exemption (IDE) must be filed with the FDA whenever research involving human subjects is conducted outside the United States with drugs, devices or biologics, which would require filing of an IND or an IDE if the research were conducted in the United States.

11.) Classified research with human subjects is held to the same ethical principles and human subject protections as unclassified research and must receive prior approval from the Secretary of Defense (SECDEF) (SECDEF Memorandum of December 13, 1999). Classified research is not eligible for review under expedited review procedures. Non-exempt classified research must be conducted following the requirements of Instruction 3216.02. DUHS does not ordinarily perform classified research. In the event a request to do so is submitted, and the research is supported or funded by DoD, the DUHS HRPP will follow the requirements of Instruction 3216.02.

12.) For collaborative multi-site research, an appropriate written agreement shall be established between the collaborators that includes a Statement of Work and specific assignment of roles and responsibilities for each party.

13.) Research on chemical and biological weapons is generally not approvable, subject to certain exceptions for prophylactic, protective, or other peaceful research. See 50 U.S.C. 1520a (reference (g)).

14.) The following shall be promptly reported to the DoD Human Research Protection Officer:
   - When significant changes to the research protocol are approved by the IRB.
   - The results of the IRB continuing review.
   - Change of reviewing IRB.
   - When the organization is notified by any Federal department, agency or national organization that any part of an HRPP is under investigation for cause involving a DoD-supported research protocol.
   - Any unanticipated problems involving risks to participants or others.
   - Any suspension or termination of DoD-supported research.

15.) When following DoD regulations and requirements, the definition of the minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests" shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in...
their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

Additional Requirements for Department of Navy (DoN) Supported Research

1.) U.S. Navy-wide survey research requires additional review. Surveys, other than those executed entirely within the command, typically require Navy Survey Review and Approval. The Navy Survey Approval Manager may require IRB review of the survey instrument prior to granting approval.

2.) Only the Surgeon General of the Navy, Commanders, and Commanding Officers may be designated as sponsors for INDs and IDEs. The Surgeon General of the Navy may consider an IND/IDE equivalency in circumstances where the requirements may not be possible or feasible in international research. Investigators may not be designated as sponsors for INDs and IDEs.

3.) Oversight by the DoN HRPP through headquarters-level review of research protocols (including relevant IRB meeting minutes) after local institutional approval and site visit of the institution’s HRPP will occur. This may be delegated to levels of command or authority appropriate to ensure compliance, and include procedures for the investigation and resolution of allegations of non-compliance, and may include procedures for headquarters-level administrative review of research. A DoD Component may delegate headquarters-level research review responsibility to another DoD Component for purposes of efficiency and consolidation of functional offices.

4.) Recordkeeping requirements include maintaining adequate documentation of DoD-supported or -conducted research involving human subjects and establishing procedures for supporting DoD reporting requirements. Recordkeeping requirements for DoN-supported research with human subjects are longer than the Common Rule’s requirement. The DoN HRPP is developing policy guidance.

5.) Reports to the DoN Human Research Protection Program (HRPP) Office and appropriate sponsor(s) must occur for:
   (a) All suspensions or terminations of previously approved DoN-supported research protocols;
   (b) The initiation and results of investigations of alleged non-compliance with human subject protections; (see added requirements in the section above on Non-Compliance)
   (c) Unanticipated problems involving risks to subjects or others, or serious adverse events in DoN-supported research;
   (d) All audits, investigations, or inspections of DoN-supported research protocols;
   (e) All audits, investigations, or inspections of the institution’s HRPP conducted by outside entities (e.g., the FDA or OHRP);
   (f) Significant communication between institutions conducting research and other federal departments and agencies regarding compliance and oversight;
   (g) All restrictions, suspensions, or terminations of institutions’ assurances.
References:

1) Department of Defense Instruction 3216.02 13, dated November 8, 2011
2) Department of Navy, Human Research Protection Program, dated February 13, 2007
3) Department of Navy, SECNAV Instruction 3900.39D, dated November 6, 2006
4) 50 U.S.C. 1520a

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