

Wayne State University Human Investigation Committee	
Subject	Department of Defense Requirements for Human Subject Research Protection
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Approvals	Administrative Approval 9/30/10

The purpose of this document is to provide guidance to Wayne State University (WSU) researchers whose human subjects' research involves any component of the Department of Defense (DoD).

Background

In the past few years, DoD components have significantly enhanced their human subjects protection requirements, including the application of those requirements to researchers who are not employees of the DoD.

WSU has signed an Addendum to its Federal-wide Assurance (FWA) that it will apply DoD regulations and policies for the protection of human research subjects when conducting, reviewing, approving, overseeing, supporting or managing human subjects research involving the DoD.

Responsibility for upholding DoD requirements for human subject research is shared between researchers and their teams, the Human Investigation Committee, University administration, and DoD.

Scope

This information and guidance applies to all biomedical and social/behavioral research which includes human subjects research and is involved with a DoD component, with the following exception: for human subjects research that qualifies for exemption see the guidance below entitled "Researcher Responsibilities – DoD Funding."

Research is considered to involve the DoD when:

- The research is funded by a component of DoD (e.g., a grant from the U.S. Army Corps of Engineers).
- The research involves cooperation, collaboration, or other type of agreement with a component of DoD (e.g., An Army Medical Laboratory will conduct malaria antigen detection tests for study).
- The research uses property, facilities, or assets of a component of DoD.
- The subject population will intentionally include personnel (military and/or civilian) from a component of DoD.

DoD policies and requirements do not apply when DoD personnel incidentally participate as subjects in research that is NOT supported by DoD, and DoD personnel are not an intended population of the research.

Research supported by the DoD and “involving a human being as an experimental subject” is subject to the Federal Policy for the protection of human subjects in research, i.e., the Common Rule. However, because of the DoD culture, organizational structure, and population, DoD Directive 3216.02 lays out additional requirements that apply as well. In the case of human research sponsored by the Department of the Navy, Secretary of the Navy Instructions (SECNAVINST 3900.39D) apply. These requirements are designed to cover risks unique to DoD employees that differ from civilians both in the conduct of research and in participation in research (e.g., deployability, personal conduct standards, and duty to report certain personnel actions). The procedures outlined in this policy ensure that WSU research supported by the DoD complies with DoD regulations governing human research.

Definitions

Department of Defense Addendum to DHHS Federal-wide Assurance: An application to the Department of Defense attesting that WSU will comply with all relevant federal regulations, DoD Instructions and Directives and other relevant documents regarding the protection of human subjects in research. The Addendum applies to research supported by the DoD, Air Force, Navy, Marine Corps, and other affiliated facilities. (Note: The Army does not use the mechanism of an Addendum. Additional Army requirements are managed through the contracting process.)

Department of Defense Component: The term *DoD component* refers collectively to the organizational entities with the DoD that are subject to the human subjects protections laid out in Department of Defense Directive 3216.02. These entities include, but may not be limited to:

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, Coast Guard Academy, 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, Tricare Health System.

Federal-wide Assurance (FWA): A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved (Federal Policy 45 CFR 46.103).

Research Monitor: A research monitor is required for Department of Defense research involving greater-than-minimal risk. The monitor must be independent of the investigative team and shall possess sufficient educational and professional experience to serve as the subject/patient advocate. The monitor shall be physicians, dentists, psychologists, nurses, or other healthcare providers capable of overseeing the progress of the research protocol, particularly with regard to issues of individual patient/subject management and safety. Note: The IRB can require the appointment of a Research Monitor for a portion of a research study or for studies involving no more than minimal risk, if deemed appropriate.

Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Experimental Subject: The Department of Defense definition is:

"An activity for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction (32CFR.210.102 (f) reference (c). 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, the withholding of an intervention that would have been undertaken if not for the research purpose."

Prisoner of War: Research involving persons considered prisoners of war (POW) (i.e., captured, detained, held under the control of DoD personnel) is prohibited. Refer to the definition of "prisoner of war" for the Department of Defense component granting the addendum. The PI is responsible for providing the HIC with the applicable definition of "prisoner of war".

- For the Army definition, see: <http://www.army-technology.com/glossary/prisoner-of-war.html>
- For the Navy definition, see: http://www.fas.org/irp/doddir/navy/secnavinst/3900_39d.pdf (Enclosure 1).

Legally Authorized Representative: Per military law and DoD Directive, informed consent may be provided by a legally-authorized representative of subjects if: (1) the subject lacks capacity due to age, condition, or other reason, to make a decision regarding consent to participate in the research AND (2) the IRB has determined that the research is intended to be beneficial to the individual subjects. (See HIC Policy "Obtaining Permission from Legally Authorized Representatives or Guardians").

HIC Policy

Research supported by the DoD and involving a human being as an experimental subject (as defined above), is subject to the Federal Policy for the protection of human subjects in research, the Common Rule in Subpart A of 45 CFR 46 under 32 CFR 219. WSU shall apply additional requirements outlined in DoD Directive 3216.02 when human research is conducted or supported by a DoD component (an organizational entity within the DoD).

The DoD applies the provisions in 45 CFR 46, Subparts B, C, and D for the protection of vulnerable classes of subjects.

The University's Federal-wide Assurance (FWA) with the Department of Health and Human Services (DHHS), Office of Human Research Protection (OHRP) meets the DoD requirement that the University maintain a federal assurance of compliance. The University shall complete a DoD addendum to its FWA when human participant research is conducted or funded by the DoD. The DoD addendum outlines the unique DoD component requirements that are not specifically included in the FWA.

HIC Procedures:

Researchers have the following responsibilities for research involving DoD:

Planning: DoD-related research typically requires additional compliance activities, documentation, and subject protections. Researchers should anticipate and plan for these requirements, which may require significant coordination of timing and activities among offices and institutions.

Budgeting: Meeting DoD requirements may increase the costs of conducting the research. DoD has provided the following guidance: "Most costs associated with Human Research Protections are expected to be included in an Institution's indirect overhead rates. However, if an Institution has identified a specific cost directly associated with performance of a particular effort and thinks the cost should be direct [sic] charted to an award, they should approach the awarding agency Contracting Officer for further consideration. The awarding agency Contracting Officer would normally make a determination as to whether this type of cost is reasonable as a direct cost to their award."

Based on the above guidance, researchers should anticipate any specific subject protection costs that might be directly associated with the project. For example, if the project involves greater-than-minimal risk to subjects and therefore requires a Research Monitor (per DoD policy), the costs associated with the monitor might qualify as direct costs. For assistance in identifying such costs and dealing with the funding agency, researchers should consult with their WSU Sponsored Programs Administrator (SPA).

DoD Funding: Researchers are not allowed to expend DoD funds for human subjects research until all of the following requirements have been met:

- The IRB has reviewed and approved the research (or granted a Concurrence of Exemption).
- WSU has furnished the Human Research Protection Program at the DoD component that is funding the research with all of the following:
 - A copy of the WSU DoD Addendum to its Federal-wide Assurance
 - Documentation of the IRB approval
 - If the research qualifies for exemption status, documentation of the exemption, including citation of the exemption category and a rationale statement.
- The WSU SPA office has received notice from the Contracting officer at the DoD component that the DoD Human Research Protection Program has reviewed the research protocol and accepted the IRB approval or exemption determination for compliance with the DoD component policies.

Waiver of Consent Requirements: If the research participant meets the definition of "Experimental Subject," waiver of consent is prohibited unless a waiver is obtained from the Secretary of Defense. If the research participant does not meet the definition of Experimental Subject, the IRB may waive consent. The requirement to obtain consent cannot be waived for any research involving the DoD, except under one of the following conditions:

- The research is intended to be beneficial to the subject, the subject lacks the capacity to provide consent, and a legally-authorized representation will provide consent. (Examples: young minors, cognitively impaired individuals.)

- The Head of the DoD component involved in the research may waive the requirement for consent with respect to a specific project in order to advance the development of a medical product necessary to the Armed Forces, but only if the research may directly benefit the subject and the research is carried out in accord with all other applicable laws and regulations (e.g., 21 CFR 50.24).
- This prohibition does NOT apply to screening (sometimes called “pre” screening) of records to identify possible subjects. The IRB can grant a waiver of consent for such activities (see HIC Department of Defense Requirements policy)
- DoD regulations prohibit an exception from informed consent in emergency medicine unless the PI obtains a waiver from the Secretary of Defense.

Research in which legally-authorized representatives (LAR’s) provide consent: Per military law and DoD directive, informed consent may be provided by a legally-authorized representative of a subject if: (1) the subject lacks capacity due to age, condition, or other reason to make a decision regarding consent to participate in the research **AND** (2) the IRB has determined that the research is intended to be beneficial to the individual subject(s). Examples of situations where LAR’s might provide consent include a parent(s) consenting on behalf of their child/ren, proxies or family members consenting on behalf of incapacitated subjects. (See HIC Policy “Obtaining Consent from Legally Authorized Representatives or Guardians”.)

Greater-than-minimal risk research: A research monitor is required for research involving greater-than-minimal risk to subjects. See DoD guidance from Department of Defense Directive 3216.2 (section 4.4.3). For research involving more than minimal risk [as defined in 32 CFR 219.102(i)] an independent research monitor shall be appointed by name. (See above definition “research monitor” as defined by the DoD).

Depending on the nature of the study, the research monitor may be assigned to assess one or more of the following phases of a research project: subject recruitment, subject enrollment, data collection, data storage, and/or analysis. At the discretion of the IRB, the research monitor may be assigned to discuss research progress with the principal investigator, interview subjects, consult on individual cases, or evaluate adverse event reports. 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 can assess the research monitor’s reports.

Protections for subjects who are military personnel: DoD **requires** certain protections for military personnel being recruited for research that involves greater-than-minimal risk. See “Research Involving Military Personnel as Research Participants” below.

Independent scientific review prior to IRB review: The **Navy** and the **Army** require independent scientific review and approval **prior to IRB review** of new applications and substantive modifications. This requirement does not apply to research involving other components of the DoD.

- A scientific review conducted by a funding agency or by an established internal review mechanism in the researcher’s school or department will satisfy this requirement. In the absence of such a review, an *ad hoc* scientific review may be provided by the researcher’s chair or dean. It may also be requested of the IRB as a step separate from the IRB review.

- Researchers may wish to look at the Naval Medical Center scientific review template and to the Army's description of scientific review criteria in its Human Research Protections Office Policies and Procedures. These are essentially the same as the scientific review conducted by any federal funding agency. An internal or *ad hoc* review should cover the same topics, including:
 - **Significance** – Does the research address a problem of scientific and/or practical importance? If the aims of the research are achieved, how will scientific knowledge be advanced? What effect will the research have upon the concepts or methods that drive this field of research? Will there potentially be important practical benefits to military and/or civilian communities? Is the research question articulated with clarity and precision? Does the background section describe why the research question is important? Is the literature review comprehensive and complete?
 - **Approach** – Are the conceptual framework, design, methods and analyses adequately developed, feasible, well-integrated, and appropriate to the aims of the study? Are the controls adequate? Does the researcher acknowledge potential problem areas and consider alternative tactics? Is the proposed sample size and statistical analysis valid?
 - **Researcher** – Is the researcher appropriately trained to conduct the research? Is the proposed work appropriate to the experience level of researcher associates?
 - **Environment** – Does the scientific environment in which the study will be done contribute to the probability of success? Does the proposed study take advantage of unique features of the scientific environment or employ useful collaborate arrangements? Are the facilities available and appropriate?

Documentation of the scientific review: The IRB must be provided with written documentation of the scientific review that summarizes the scientific issues raised and addressed during the review, together with a statement that names and describes the reviewers. Appropriate documentation might include a copy of a review summary from a federal agency, or a memo from the researcher's department chair.

Education and training requirements: The DoD education and training requirements may **exceed** requirements of WSU. Initial education and training is described by the DoD as follows: "all personnel involved in reviewing, approving, supporting, conducting, managing, or overseeing research involving human subjects must complete initial and ongoing research ethics and human subjects protections training appropriate to each individual's level of involvement, duties, and responsibilities." [Secretary of Navy, SecNav Instruction 3900.39D]. (Note: WSU mandated online CITI training must also be completed.)

DoD requires continuing education **every year**. Researchers and appropriate research staff should plan to take the refresher modules through CITI for this purpose.

Multi-site or collaborative research requirements – A PI developing a proposal for DoD funding or other support that involves other collaborating institutions should first consult the DoD component early in the proposal development process to identify additional requirements for multi-site research, including identification of the roles and responsibilities of each party. In order to ensure consistent protection of subjects under DoD requirements, a PI conducting DoD-sponsored multi-site research must submit information to the IRB on the FWA(s) held by the collaborating institutions, including the existence of any DoD addendum or other direct DoD assurance. A formal agreement between the organizations is required to specify the roles and responsibilities of each party.

Conducting international research – In addition to HIC policy, DoD-related research that involves subjects who are not U.S. citizens or Department of Defense personnel requires the following:

- Permission of the host country.
- Ethics review and approval by the host country or by a local Naval IRB with host country representation.

Documentation responsibilities: Researchers are required by DoD policy to maintain an extensive number of research-related and compliance-related documents in their files. Researchers should contact the specific DoD component funding the research for specifics on these requirements.

Provisions for Research-Related Injuries: For DoD sponsored research, DoD components may have stricter requirements than the Common Rule requirements for research-related injuries. The IRB shall apply the stricter requirements for research-related injuries as outlined by the DoD component conducting or supporting the research.

Research Involving Military Personnel as Research Participants: When research involves U.S. military personnel, additional protections for military research participants are required to minimize undue influence.

1. In cases where the research involves U.S. military personnel as subjects, the principal investigator (PI) must submit with the IRB application a plan for research subject recruitment that incorporates additional safeguards to minimize undue influence from individuals within a potential subject's chain of command. The PI should consult the sponsoring DoD component, as necessary, for assistance.
2. For research involving greater-than-minimal risk to subjects *and* involving military personnel, the PI must include procedures in the subject recruitment plan to ensure that officers cannot influence the decision of their subordinates to participate in the research.
3. The PI must include in the IRB application his/her procedures of subject recruitment to ensure that officers and senior or other non-commissioned officers cannot be present at the time of recruitment or consent of their subordinates.
4. The PI must provide a separate opportunity or recruitment session for officers and senior non-commissioned officers to participate as research subjects.
5. For studies in which subject recruitment involves a percentage of a unit, the PI must ensure an independent ombudsman shall be present during the recruitment process to monitor the voluntary nature of participation and that information provided is adequate and accurate.
6. Unless on leave status during research participation, military personnel may not receive compensation for their participation. The IRB reviews the proposed subject compensation to ensure that the PI does not violate DoD policies limiting dual compensation for U.S. military personnel:
 - a. An individual may not receive pay from more than one position for more than 40 hours of work in one calendar week.
 - b. Limits address temporary, part-time, and intermittent appointments
7. WSU does not apply DoD policies when U.S. military personnel incidentally participate as subjects in a study that is not DoD-sponsored or supported and U.S. military personnel are not the intended target population.

Additional DoD Review Required Prior to Initiation of Study:

After the IRB completes its review and issues approval, the PI must submit documentation of IRB approval to the DoD Component sponsoring or supporting the study. This approval must include the risk level and expiration date of the research.

The DoD may also request additional documentation to verify compliance with federal and DoD policies, including minutes related to the research.

The PI may not initiate the study until the human research protection officer within the sponsoring DoD component reviews and approves the IRB approval and other submitted documentation.

Post-IRB Responsibilities:

- Continuing education – as described above, the DoD requires annual continuing education related to human subjects for the researchers and appropriate research staff.
- Research results – DoD requires that the researcher provide the IRB with copies of publications, presentations, and reports resulting from the research.
- The DoD may require research records be submitted to the DoD for archiving.
- Modifications to the research – DoD requires that all substantive amendments to approved DoD research (e.g., new procedures, a new subject population, a new aim) involving human subjects receive scientific review **prior** to IRB review. This can be done by the Department Chair or his/her designee.
 - When preparing an Amendment Form to the HIC for review, the researcher is responsible for reviewing the Protocol, Protocol Summary Form, consents, and other applicable documents to ensure that they accurately reflect the research.
 - If the research was not previously DoD-related, but the Amendment will make it DoD-related, the researcher must submit all DoD-required information along with the Amendment Form, per HIC Amendment Form directions.
- Reporting obligations – The researcher is responsible for notifying DoD and the HIC of any audits, investigations, or inspections of DoD-related research.

References

45 CFR 46 Title 45 Code of Federal Regulations, part 46 (45 CFR 46) is the primary set of Federal regulations regarding the protection of human subjects in research and is often referred to as the **Common Rule**. It defines the laws, criteria for exemption, as well as definition and formulation of Institutional Review Boards (IRB's). Some Government agencies (e.g., DoD, FDA, etc.) have established their own implementation of this code that supersedes portions or all of 45 CFR 46. See <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>

32 CFR 219 This is the Department of Defense (DoD) implementation of 45 CFR 46, Subpart A. Subparts B, C, and D of 45 CFR 46 still apply to DoD supported research. It differs from 45 CFR 46 in the criteria for exemptions.

DoD Directive 3216.02 This document defines additional requirements for human subject research supported by the Department of Defense. See <http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf>

10 USC 980 Title 10, United States Code, Subtitle A, Part II, Chapter 49, Section 980 (10 USC 980) addresses the limitations on use of humans as experimental subjects. It basically states that funds cannot be deployed prior to obtaining informed consent. See http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=browse_usc&docid=Cite:+10USC980

21 CFR 50.24 This document addresses the Food & Drug Administrations, Department of Health & Human Services, Part 50, Subpart B, Informed Consent of Human Subjects. See <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=50.24>