



MCW Office of Research Standard Operating Procedure

RESEARCH INVOLVING DEPARTMENT OF DEFENSE FUNDING AND/OR MILITARY PARTICIPANTS

Unit: Human Research Protections Program (HRPP), Office of Research

Applies to: Faculty and Staff involved in human research

PURPOSE:

Research under the review of the Medical College of Wisconsin (MCW) Institutional Review Board (IRB) and sponsored by the Department of Defense (DoD), or involving collaboration with the DoD, or DoD facilities or personnel both military and civilian must meet additional requirements including special protections for research subjects, as well as additional review and reporting requirements.

This procedure outlines the general requirements for projects funded by a DoD component, cooperation, collaboration, or other agreement with the DoD, using property, facilities, or assets of a DoD component, or involving military or civilian personnel from a DoD component which are required in addition to MCW IRB's policies and procedures.

This procedure does not apply to non-DoD research projects where US military personnel are only incidentally enrolled as subjects.

DEFINITIONS:

DoD Component: A component involves one or more of the following agencies or offices: Office of the Secretary of Defense (OSD), the Military Departments, the Office of the Chairman of the Joint Chiefs of Staff and the Joint Staff, the Combatant Commands, the Office of the Inspector General of the Department of Defense, the Defense Agencies, the DoD Field Activities.

- This also includes all other organizational entities within the Department of Defense including but not limited to: Air Force, Air Force Academy, Army, Army Corps of Engineers, Coast Guard, Coast Guard Academy, Defense Advanced Research Projects Agency (DARPA), Defense Intelligence Agency, Military Academy (West Point), Missile Defense Agency, National Geospatial-Intelligence Agency, National Guard, National Security Agency, National War College, Navy, Naval Academy, Office of Naval Research, Pentagon Force Protection Agency, Tricare Health System, U.S. Naval Observatory.

Substantive Modifications: MCW HRPP defines a substantive modification as a change in principle investigator, change or addition of an institution, elimination or alteration of the consent process, change to the project population that has regulatory implications (e.g. adding children, adding active duty population, etc.), significant change in project design warranting additional scientific review, or a change that could potentially increase risks to subjects.

Detainee: Any individual captured by, or transferred to the custody or control of, DoD personnel pursuant to the law of war. This does not include persons being held solely for law enforcement purposes, except where the United States is the occupying power. Detainees who are U.S. citizens or U.S. resident aliens will continue to enjoy all applicable rights and privileges under U.S. law and DoD regulations.

Classified Research: Federally sponsored research in which all or some portion of the project, or knowledge of the procedures or results of which, are restricted or require security clearance as dictated by the U.S. Government.

Experimental Subject: Subjects included in an activity for research purposes where there is intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction.

Minimal Risk Research: Research where the probability and magnitude of physical or psychological harm is that which is ordinarily encountered in daily life, or during the performance of routine physical or psychological examinations or tests. For research involving the DoD, the phrase “ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life, for example, inherent risks encountered by emergency responders, pilots, soldiers in a combat zone, or subjects with a particular medical condition.

Research Monitor: An individual with expertise consonant with the nature of risk(s) identified within a research protocol and whose role is to protect the safety and well-being of human subjects.

POLICY:

1. Investigators who receive support, collaborate with DoD Components, or enroll military and/or civilian personnel for their research must comply with MCW policies in the review and conduct of human subject research.
2. In addition, Investigators should review and apply the additional requirements described in this policy.

Training Requirements:

1. The DoD requires that all individuals involved in the design, conduct, and approval of human subject research complete human subject research protections (HSRP) training. *See IRB SOP: Human Subject Research Protections Training Requirements* for more information regarding MCW IRB requirements for DoD supported research.
2. In addition to this training, the Department of Navy (DON), including the Marine Corps, requires that investigators, institutional and IRB leadership complete the additional CITI Training Module for DON-Supported Extramural Performers. Refresher training must be completed every three years.
3. Investigators and research staff involved with projects sponsored by the Secretary of Defense are required to complete annual HSRP training.

Scientific Review:

1. For research projects involving the Army or Navy (including the Marine Corps) additional documentation of independent scientific review prior to IRB review of new applications and substantive modifications is required. This scientific review may be

provided by the funding agency, by an established internal review mechanism within the investigator's academic unit, or through an ad hoc scientific review by the investigator's chair or dean. Evaluation of scientific merit conducted by the IRB as part of its review may be sufficient in some cases, as well.

2. Scientific review should include the name and qualifications of the reviewer(s) and must demonstrate that the research uses procedures consistent with sound research design and is likely to yield the expected results. Additionally, the scientific review must include an assessment of the following elements:
 - Significance of the research question.
 - Scientific approach;
 - Research team qualifications;
 - Facilities and resources available;
3. Amendments not meeting the criteria to be considered a substantive modification should include documentation that additional scientific review is not needed.

Surveys and Interviews:

1. Research involving surveys or interviews with DoD military or civilian personnel, or their families may require additional DoD approval.
2. Documentation from the DoD component should be provided regarding any additional review requirements along with the timing of the review.

IND/IDE Restrictions:

1. Investigators conducting research involving the Navy may not be designated as sponsors of an Investigational New Drug (IND) or Investigational Device Exemptions (IDE).
 - a. Only the Surgeon General, Commanders, and Commanding Officers may act as sponsors of an IND or IDE.

International Research:

1. For DoD research conducted outside of the United States, the Investigator and IRB must consider the laws and requirements of the host country as well as the cultural context of the research. In conduct of such research, the laws, customs, and practices of the country in which the research takes place or those required by the regulations at 32 CFR § 219.101, whichever are more stringent, will take precedence.
2. The research must meet the same standards of ethics and safety that apply to research conducted within the United States involving U.S. citizens, and will be conducted in accordance with applicable international agreements.
 - a. This may be documented via an in-country or IRB/ethics review and/or a review by a consultant with expertise in that country as described in *IRB SOP: International Research*.
3. For Navy research involving subjects who are not US citizens or DoD personnel, the investigator must provide documentation of permission from the host country and an ethics review and approval by the host country or local Naval IRB with host country representation.

Collaboration:

1. Collaborating institutions in multi-site research must have a Federal Wide Assurance (FWA) with Office of Human Research Protections (OHRP). Investigators must provide documentation of IRB approval or establish an IRB Authorization Agreement for collaborators. Investigators who would like to establish an IRB authorization should review and follow *IRB SOP: Reliance Agreements for Multi-Site Projects*.

2. The roles and responsibilities of each institution must be specified in any such agreement along with a statement by which the parties agree to comply with any special DoD requirements.

Force Health Protection:

When using an IND under a force health protection program, the DoD components involved in implementation shall provide prior notice to personnel receiving the drug or biological product and provide all pertinent clinical information to health care providers who administer the IND.

Prohibited Research:

1. Research with detainees (prisoners of war), except research with investigational new drugs or devices where such treatment would also be offered to US military service members at the same location and with the same medical condition consistent with established medical practice.
2. Research involving human testing of chemical or biological agents is prohibited, except for certain prophylactic, protective or peaceful purposes.

Classified Research:

Written permission to engage in classified research must be granted by the Dean of the Medical College of Wisconsin (MCW) (or designee) prior to engaging in such work and prior to the submission of applications for grants, contracts, or regulatory permission to conduct the work.

DoD Limitations on Waivers of Informed Consent and Consent by Legally Authorized Representatives (LAR):

1. Consent cannot be waived for any research using DoD funds and meeting the definition of research involving a human being as an experimental subject according to 10 USC 980.
2. This places limitations on research involving deception, decisionally-impaired individuals, or research being conducted under emergency conditions where the subject may not be able to provide consent.
 - a. This does not apply to retrospective research involving analysis of data or specimens, observational projects, blood draws, or tissue collection, and does not apply to screening of records to identify potential subjects for activities such as these, the IRB may grant a waiver of consent.
3. This consent requirement may be waived by the Assistant Secretary of Defense for Research and Engineering for 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.
4. For research involving a human being as an experimental subject, informed consent must be obtained from the subject or the subject's LAR. Informed consent may be provided by a LAR only if the subject lacks decision-making capacity and the IRB has determined that the research is intended to be beneficial to the individual subjects.

Inclusion of Subject Populations:

The selection of human subjects must reflect gender and minority participation in DoD projects in accordance with public law 103-160 § 252. The requirement to include women and minorities may be waived by the Secretary of Defense if the Secretary determines that the project is inappropriate with respect to the health of subjects,

inappropriate with the purpose of the research, or inappropriate under such other circumstances as the Secretary of Defense may designate.

Research Monitor:

1. A research monitor must be appointed for all research considered more than minimal risk. The monitor should be independent of the team conducting the research involving human subjects.
 - a. The monitor's duties may include observation of recruitment, enrollment, and the consent process, as well as reviewing safety monitoring and overseeing data collection and analysis.
 - b. The monitor shall have the authority to take necessary steps to protect the safety and well-being of human subjects by stopping research in progress until the IRB can assess the monitor's report.
 - c. The monitor must promptly report observations and findings to the IRB or other designated official and the HRPO.
2. The Investigator must identify the monitor by name, provide a written summary of the monitors' duties, authorities, and responsibilities, and the selection must be approved by the IRB.
 - a. More than one monitor may be appointed even if the research is deemed to be no more than minimal risk.

Protections from Medical Expenses:

1. For any research projects considered to be more than minimal risk, the informed consent document must provide an explanation as to whether any compensation and any medical treatments are available if injury occurs, what they consist of and where further information may be obtained.
2. For Navy research project involving more than minimal risk, the project must include an arrangement for emergency treatment and necessary follow-up of any research-related injury. The project application must specify whether any compensation is available if injury occurs and a plan for emergency treatment and necessary follow-up of any research-related injury.

DoD Personnel as Research Subjects:

1. Adult Status: The age of majority in the state of Wisconsin is eighteen years; however, in DoD research projects, active duty service members and reserve component members are considered to be adults even if they are under the age of eighteen.
2. Command Approval: As it may impact readiness in the field, command approval may be required prior to military personnel participating in human subject research. Investigators must provide documentation of command approval in the form of an attached letter of agreement indicating that the investigator has permission to conduct the research. Civilian researchers attempting to access military volunteers should seek collaboration with a military research familiar with service-specific requirements.
3. Protection of Service Members from Undue Influence: Officers and senior non-commissioned officers may not influence the decisions of subordinates to participate in human subject research and may not be present at the time of recruitment. Superior officers must be recruited in a separate session from subordinates. Military

status of any research team members obtaining consent must be documented in the project application in order for the IRB to assess this requirement.

- a. For research considered more than minimal risk and where recruiting is conducted in a group setting, an ombudsman must be present to ensure information is clearly, accurately, and adequately presented and the voluntary nature of participation is emphasized. A research monitor may act as ombudsman.
4. **Civilian Personnel:** DoD civilian personnel recruited for research shall be afforded the same protections as military personnel. The requirement of an ombudsman is at the discretion of the IRB.

Additional Reporting Requirements:

Determinations of serious or continuing noncompliance, unanticipated problems involving risks to subjects or others, project suspensions or terminations, audits, inspections or investigations of DoD research, results of continuing review, changes to the reviewing IRB, and substantive amendments to the protocol (reviewed and approved by the HRPO prior to implementation) must be promptly reported to the HRPO within 30 days of the event.

Limitations on Compensation:

1. Human subjects who are non-federal civilian personnel (i.e. contractors) may be compensated up to \$50 for blood draws. Compensation is allowed for general research participation if approved by the IRB. Payment may come from a federal or non-federal source.
2. On-duty federal personnel including military members may be compensated up to \$50 for blood draws, but compensation is not allowed for general research participation.
3. Off-duty federal personnel including military members may be compensated up to \$50 for blood draws. Compensation is allowed for general research participation, if approved by the IRB; however, payment may not come directly from a federal source. Payment from a federal contractor or non-federal source is permissible.
4. Compensation paid to DoD employees, both military and civilian, must comply with the requirements in the DoD Instruction 3216.02 § 11. Investigators who plan to compensate subjects may need to inquire about their military status in order to comply with these requirements. Investigators should describe their plan for assessment of military status.

Record Keeping:

1. To be consistent with MCW policy, research records should be maintained for a minimum of 10 years after the completion of the research; however, individual DoD components may have additional requirements, including the transfer of records to the DoD.
2. If the DoD requires that research records be transferred to the DoD component, MCW should retain the original copy of the research record and provide a copy to the DoD component unless there is an executable data usage agreement specifying otherwise.
3. Retained records should be made accessible for inspections and copying by authorized representatives of the DoD.

REFERENCES:

Department of Defense Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research, November 8, 2011
Department of Defense Instruction 3210.7, Research Integrity and Misconduct
Department of Defense Instruction 6200.2, Use of Investigational New Drugs in Force Health Protection
10 USC 980, Limitations on the Use of Humans as Experimental Subjects
32 CFR 219, Protection of Human Subjects
103-160 § 252
HA Policy 05-003, Policy for Protection of Human Subjects in Department of Defense Sponsored Research
AR 70-25, Use of Volunteers as Subjects of Research, January 25, 1990
AR 40-38, Clinical Investigation Program, September 1, 1989
AR 40-7, Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances, October 19, 2009
SECNAV Instruction 3900.39D, Human Research Protection Program, November 6, 2006
Air Force Instruction 40-402, Protection of Human Subjects in Research

SUPPORTING DOCUMENTS:

IRB SOP: Human Subject Research Protections Training Requirements
IRB SOP: International Projects
IRB SOP: Reliance Agreements for Multi-Site Projects

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