1. Introduction

Research sponsored by the Department of Defense (DoD) involving collaboration with DoD or involving DoD facilities or personnel (military or civilian), is subject to additional requirements including special protections for research participants, as well as additional review and reporting requirements for investigators and IRBs. Investigators should review these requirements when planning a DoD-supported research project as they may add a significant amount of time to the review and approval process of research.

The focus of this guidance document is on requirements outlined in DoD Instruction 3216.02 (DoDI 3216.02), Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research (November 8, 2011). For a checklist of investigator responsibilities related to DoD sponsored research, see the DoD PI Checklist.

Each DoD Component (e.g., Army, Navy, Air Force) may have additional requirements beyond those included in this guidance document. Principal investigators are advised to check with their sponsoring Component program manager about any additional requirements.

2. When is Human Research Subject to DoD Special Requirements?

Human research must comply with DoD requirements when:

- The research is funded by a DoD Component, including cases where U-M is the recipient of a subaward from the direct recipient of DoD funds, or
- The research involves cooperation, collaboration or other type of agreement with a DoD Component, or
- The research uses property, facilities, or assets of a DoD Component, or
- The participant population will intentionally include personnel (military and/or civilian) from a DoD Component. (DoD requirements do not apply when DoD personnel incidentally participate in research where they are not the intended research population or where the project is not DoD-supported).


Upon completion of U-M IRB review and approval, including determination of exempt or not IRB regulated status, the HRPO for the sponsoring component must perform an administrative review of the research before activities with research participants may begin. The review involves confirmation that the University and the proposed research are in compliance with DoD requirements for the protection of research participants. If research will be conducted in a foreign country, the administrative review will also ensure compliance with any applicable laws and requirements and cultural sensitivities of a foreign country. While the HRPO review is not an IRB review, the HRPO may require changes to the research prior to the start of the research. The Principal Investigator is responsible for submitting the information required by the sponsoring Component.
4. Special Requirements for IRB Review of DoD Research

4.1 Training Requirements
DoD requires that all individuals involved in the “design, conduct, or approval of human subjects research” complete initial and continuing human subjects research education and training. There might be specific DoD educational requirements or certification required by different DoD components.

U-M PEERRS Human Subjects Research Protections training, renewable every three years, meets the training requirements for many DoD Components. Investigators are responsible for ensuring that all study team members engaged in the conduct of research complete PEERRS. The DoD Component may evaluate the institution’s training program to ensure that personnel are qualified to perform the research, based upon the complexity and risk of the research.

Component specific training:
All investigators and research staff on projects sponsored by the Secretary of Defense Office of the Secretary of Personnel and Readiness are required to complete annual human subjects protections training. Completion of PEERRS training annually satisfies this requirement.

4.2 Scientific Review
The IRB must consider the scientific merit of the research during their review. The IRB may rely on outside experts to provide an evaluation of scientific merit.

The scientific review may be the review provided by the funding agency (including DoD), by an established internal review mechanism in the researcher’s academic unit, or in the form of an ad hoc review by the researcher’s chair or dean. In some cases, the evaluation of scientific merit that is conducted by the IRB as part of its review is sufficient. The IRB or DoD program manager can assist with the determination of the appropriate review mechanism.

If required, documentation of the scientific review must be provided to the IRB at the time the IRB application is submitted and for substantive amendments. Scientific review must demonstrate that the research uses procedures consistent with sound research design and is likely to yield the expected results and should include the assessment of the following elements:

- Significance of the research question;
- Scientific approach;
- Research team qualifications; and
- Facilities and resources available.

The name and qualification of the reviewer(s) should be included as part of the review.

4.3 DoD Approval of Surveys/Interviews
Research involving surveys or interviews with DoD personnel (military or civilian) or their families may require DoD approval after the research protocol is reviewed and approved by the IRB. When a survey crosses DoD Components, additional review is required. The DoD
Component program manager can confirm any additional review requirements and the timing of the review (before or after IRB review). Documentation of this review must be provided to the IRB.

4.4 International Research
In its review of research conducted outside of the United States, the IRB must confirm that all national laws and requirements of the foreign country have been met and consider the cultural sensitivities in the setting where the research will take place.

The investigator must:
- Obtain permission to conduct research in that country by certification or local ethics review; and
- Follow all local laws, regulations, customs and practices.

4.5 Collaboration with other Institutions
Collaborating institutions in multi-site research must hold a federalwide assurance. Study teams must provide the following:
- Documentation of IRB approval or IRB Authorization Agreement for engaged collaborators; and
- A statement of compliance with special DoD requirements (See the U-M DoD addendum).

5. Unique Human Subject Protections Required for DoD-related Research

5.1 Prohibited Research
- 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.

DoD Instruction 2310.01E defines a detainee as: “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 human subjects research: by policy, U-M does not conduct classified research.

- Human testing of chemical or biological agents, except for certain prophylactic, protective or peaceful purposes.

5.2 Definition of “Experimental Subjects”
10 USC 980 provides a special definition for experimental subjects as those 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.” Research involving a human being as an experimental subject is a subset of research involving human participants.

5.3 DoD Limitations on Waivers of Informed Consent and Consent by LARs

The Common Rule identifies conditions where an IRB may waive consent for DoD-conducted and DoD-supported research involving humans as research participants. However, the requirement to obtain consent cannot be waived for any research using DoD funds and meeting the definition of research involving a human being as an experimental subject (see section 5.2 above). This places limitations on research involving deception, decisionally-impaired individuals, or research being conducted under emergency conditions where the participant may not be able to provide consent.

When the research meets the 10 USC 980 definition of research involving a human being as an experimental subject, informed consent must be obtained in advance from the participant or the participant’s legal representative consistent with the Common Rule if the participant cannot consent. Informed consent may be provided by a legally authorized representative (LAR) only if: (1) the research participant lacks decision-making capacity; AND (2) the IRB has determined that the research is intended to be beneficial to the individual research participants.

This statute applies only to certain intervention studies. It does not apply to retrospective research involving analysis of data or specimens, observational studies, blood draws, or tissue collection, and does NOT apply to screening of records to identify possible research participants. The IRB may grant a waiver of consent for such activities.

The Secretary of Defense may waive this consent requirement 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 research participant and the research is carried out in accordance with all other applicable laws and regulations.

5.4 Definition of Minimal Risk

The definition of minimal risk that includes the phrase “ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests” must not be interpreted to include the inherent risks that certain individuals face in their everyday lives. For example, the risks imposed in research involving a special population should not be evaluated against the inherent risks encountered in the research participant’s 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).

5.5 Research Monitor for Greater than Minimal Risk Research

A research monitor must be appointed for all research that involves greater than minimal risk. The monitor may be either a medical or non-medical monitor depending on the nature of the research. The monitor must be independent of the research team and possess sufficient expertise to evaluate the risks and conduct of the research. The investigator must identify a research monitor by name and have the selection approved by the reviewing IRB. The IRB may choose to appoint more than one monitor for a project and may choose to appoint a
monitor for research that is deemed to be no more than minimal risk. The monitor may be an ombudsman or a member of the data safety monitoring board.

The duties of the monitor are determined based upon the specific risks or concerns associated with each research project. The research monitor may perform oversight functions (e.g., assessment of participant recruitment, enrollment, and the consent process; oversee study interventions and interactions; review monitoring plans and unanticipated problems involving risks to participants or others; and oversee data matching, data collection and analysis) and report their observations and findings to the IRB. The monitor may be asked to discuss the research protocol with the investigator, interview participants, and consult with others outside of the study. The monitor has the authority to stop a study in progress, remove participants from the study, or take necessary steps to protect the safety and wellbeing of participants until the IRB can assess the study.

The IRB must document the required duties, authorities, and responsibilities of the monitor and communicate this information to the monitor.

The Heads of the Office of the Secretary of Defense and DoD Components may waive the requirement for the monitor on a case-by-case basis when the inclusion of a research monitor is not necessary to provide additional protections for human subjects.

5.6 Vulnerable Populations
DoD requires that the protection of Common Rule Subpart B (Pregnant Women/Fetuses), C (Prisoners), and D (Children) be applied to the research it supports. The DoD (and the IRB) considers the need for similar safeguards for other vulnerable populations such as those with cognitive impairment, mental illness, physical disability or any other circumstance that might require special protections.

For research involving pregnant women, fetuses, and neonates as participants:
- For purposes of applying Subpart B, the phrase “biomedical knowledge” is 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 includes interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.

For research intending to include prisoners as participants:
- Research intending to include prisoners as participants cannot be reviewed by the IRB through an expedited review procedure.
- When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum. The prisoner representative may be a prisoner, an employee of the prison, or an individual not affiliated with the prison.

Categories of allowable research involving a prisoner:
In addition to allowable categories of research on prisoners identified in Subpart C, epidemiological research is also allowable when:
1. The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor associations for a disease.
2. The research presents no more than minimal risk.
3. The research presents no more than an inconvenience to the participant.

When a participant becomes a prisoner:
- When a previously enrolled participant becomes a prisoner and the relevant research protocol was not reviewed and approved by the IRB in accordance with the requirements of subparagraphs 7.b.(1) and (2) of DoD 3216.02, the principal investigator must promptly notify the IRB.
- If the principal investigator asserts to the IRB that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner, the IRB Chair may determine that the prisoner-participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the IO and DoD Component office review the IRB’s approval to change the research protocol. Otherwise, the IRB Chair must require that all research interactions and interventions with the prisoner-participant (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 participant has become a prisoner, must promptly re-review the research protocol to ensure that the rights and wellbeing of the participant, 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-participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-participant’s confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-participant to continue to participate in the research. This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.

For children as participants:
- Research involving children must meet the additional relevant protections of Subpart D.
- The exemption of 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.

Section 6 below describes protections for military personnel as research subjects.

**5.7 Informed Consent Element Requirements**
Consent documents must include additional DoD elements of disclosure:
Guidance: Additional Requirements for Department of Defense (DoD) Sponsored Research

- A statement that the DoD or a DoD organization is funding the study, unless the research involves no more than minimal risk. The Secretary of Defense may grant an exception to this requirement on the grounds that providing this information could compromise intelligence sources or methods.
- A statement that representatives of the DoD are authorized to review research records.
- The disclosure for research-related injury must follow the requirements of the DOD component.

6. DoD Personnel as Research Subjects

6.1 Military Participants

- **Adult Status**: All active duty service members and reserve component members are considered to be adults for the purpose of participating in DoD-conducted or supported research.

- **Command Approval**: Command approval may be required for military personnel to participate in research as some types of research could impact a soldier’s readiness in the field. Investigators may be asked to provide documentation of Command approval as part of the IRB review. Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.

- **Protection of Service Members from Undue Influence**: Superiors (e.g., military and civilian supervisors, unit officers and noncommissioned officers (NCOs)) may not influence the decision of subordinates to participate in research and may not be present at the time of recruitment. Superior officers must be recruited in a separate session from subordinates.

  For greater than minimal risk research and where recruitment is conducted in a group setting, an ombudsman must be present to ensure that information is clearly, accurately and adequately presented and that the voluntary nature of participation is emphasized. The ombudsman may be the same individual appointed by the IRB as the research monitor.

6.2 DoD Civilian Personnel

DoD civilian personnel who are recruited into research are afforded the same protections as military personnel (6.1 above). When recruitment of civilians occurs in a group setting, the IRB must discuss appointing an ombudsman for the purposes described above. The decision to require the appointment of an ombudsman should be based in part on the human subject population, the consent process, and the recruitment strategy.

6.3 Limitations on Compensation

When human participants are on-duty federal personnel including civil servants or military members:

- Compensation of up to $50 is allowed for blood draws
- Compensation is not allowed for general research participation.
Guidance: Additional Requirements for Department of Defense (DoD) Sponsored Research

When human participants are off-duty federal personnel including civil servants or military members:

- Compensation of up to $50 is allowed for blood draws;
- Compensation is allowed for general research participation, as approved by the IRB. Payment many not come directly from a federal source. Payment from a federal contractor or non-federal source is permissible.

When human participants are not federal personnel:

- Compensation of up to $50 is allowed for blood draws;
- Compensation is allowed for general research participation, as approved by the IRB. Payment may come from a federal or non-federal source.

7. Other DoD-Specific Requirements

7.1 Reporting Requirements

The following must be promptly reported to the HRPO (no longer than within 30 days of the event):

- Determinations of serious or continuing non-compliance;
- Unanticipated problems involving risks to participants or others;
- Study suspensions or terminations;
- Audits, inspections or investigations of DoD research;
- Results of Continuing Review;
- Changes to the reviewing IRB;
- Substantive modifications to the research protocol including: a change in Principal Investigator, change or addition of an institution, elimination or alteration of the consent process, change to the study population that has regulatory implications (e.g. adding children, adding active duty population, etc.), significant change in study design that would prompt additional scientific review, or a change that could potentially increase risks to participants. Amendments must be reviewed and approved by the HRPO prior to implementing the change to the study.

7.2 Recordkeeping

Consistent with U-M policy, research records must be maintained for at least 3 years after the completion of the research. The DoD may require that research records be transferred to the DoD Component rather than being retained by U-M.

Records that document compliance or noncompliance with DoD regulations must be made accessible for inspection and copying by authorized representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD Component.
Guidance: Additional Requirements for Department of Defense (DoD) Sponsored Research

References*

DoD Regulations and Guidance

32 CFR 219, Protection of Human Subjects

10 USC 980, Limitations on the Use of Humans as Experimental Subjects

DoD Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research

DoD Instruction 3210.7 Research Integrity and Misconduct

DoD Instruction 6200.2, Use of Investigational New Drugs in Force Health Protection

DoD Component Requirements

Department of the Army

AR 70-25: Use of Volunteers as Subjects of Research

AR 40-38: Clinical Investigation Program

AR 40-7: Use of U.S. Food and Drug Administration-Regulated Investigational Products in Humans including Schedule I Controlled Substances

Department of the Air Force

Air Force Instruction DODI3216.02_AFI40-402: Protection of Human Subjects and Adherence to Ethical Standards in Air Force Supported Research.

* The DoD regulatory and guidance resources cited here are key resources regarding the conduct of DoD-related human subjects research. This is not intended to serve as an authoritative list of all regulations or guidance that may apply to such research. The sponsoring DoD Component can provide additional information.