Guidance: Additional Requirements for Department of Defense (DoD) Human Subjects Research

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 human subjects review and approval process throughout the research.

The focus of this guidance document is on requirements outlined in DoD Instruction 3216.02, *Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research* (November 8, 2011) and in Navy guidance SECNAV Instruction 3900.39D, *Human Research Protection Program* (November 6, 2006). 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 (Attachment A), 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 subject population will intentionally include personnel (military and/or civilian) from a DoD Component. (DoD requirements do not apply when DoD personnel incidentally participate as research subjects where they are not the intended research population or where the project is not DoD-supported).

3. Required DoD Human Research Protections Office (HRPO) Administrative Review

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 human subjects may begin. The review involves confirmation that the University and the proposed research are in compliance with DoD requirements for the protection of human subjects. 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 human subjects research training. U-M PEERRS human

subjects 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 human subjects 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

Research involving components of the Army or Navy (including Marine Corps) may require documentation of scientific review prior to IRB review of new applications and substantive amendments.

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. 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 the research conducted outside of the United States, the IRB must consider the laws and requirements of the host country as well as the cultural context of the research. This typically requires documentation of a review by an in-country IRB or ethics committee and/or a review by a consultant with expertise in that country.

For Navy-sponsored research involving subjects who are not US citizens or DoD personnel, study teams must provide the following documentation:

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

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."

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

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 (10 USC 980). 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.

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 subjects. 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 subject and the research is carried out in accordance with all other applicable laws and regulations.

Informed consent may be provided by a legally authorized representative (LAR) only if: (1) the subject lacks decision-making capacity; AND (2) the IRB has determined that the research is intended to be beneficial to the individual subjects.

5.4 Definition of Minimal Risk

The DoD Instruction cautions that the Common Rule definition of minimal risk that includes the phrase "ordinarily encountered in daily life or during the performance of routine physical or psychological tests" must not be interpreted to include the inherent risks that certain individuals face in their everyday lives, such as a soldier in a combat zone or an individual who has a particular medical condition.

5.5 Research Monitor for More than Minimal Risk Research

A research monitor must be appointed for all research that involves more 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 duties of the monitor are determined based upon the specific risks or concerns associated with each research project. Examples of monitor activities include assessment of subject recruitment and enrollment, data collection or data storage, and analysis. The monitor may be asked to discuss research progress with the investigator, interview subjects, or evaluate adverse events. 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 well-being of participants until the IRB can assess the study.

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

The Institutional Official of the DoD Component may waive the requirement for the monitor.

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. See DoD Instruction 3216.02, Part 7, for a description of additional DoD considerations for these populations. 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.

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

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5.7 DoD Protections from Medical Expenses if Injured

For more than minimal risk research, the informed consent document must provide information regarding payment of medical expenses, provision of medical care, or compensation for research-related injuries, consistent with the requirements of the Common Rule.

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 human subjects 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.

- **Protection of Service Members from Undue Influence:** Officers and senior non-commissioned officers may not influence the decision of subordinates to participate in human subjects research and may not be present at the time of recruitment. Superior officers must be recruited in a separate session from subordinates.

  For more 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). The requirement for an ombudsman is at the discretion of the IRB.

6.3 Limitations on Compensation

On-duty federal personnel including military members:

- Up to $50 for blood draws;
- Compensation is not allowed for general research participation.

Off-duty federal personnel including military members:

- Up to $50 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.

Non-federal personnel:

- Up to $50 for blood draws;

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- 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 (within 30 days of the event):

- Determinations of serious or continuing noncompliance;
- Unanticipated problems involving risks to subjects 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 subjects. 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.

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References*

U-M DoD/Navy Addendum

Department of Defense – Navy Addendum to the Federalwide Assurance for the Protection of Human Research Subjects (University of Michigan, June, 27, 2014)

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

Office of the Secretary of Defense for Personnel and Readiness (download)

HA Policy 05.003: Policy for Protection of Human Subjects in Department of Defense Sponsored Research

Department of the Army (copy into a browser)

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 Navy

SECNAV Instruction 3900.39D, Human Research Protection Program, November 6, 2006

Department of Navy, Training and Education Guidance, March 2013.

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.

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Attachment A – Major DoD Components**

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

** This is not a comprehensive list of DoD Component entities.