Guidance: Additional Requirements for Department of Defense (DoD) Sponsored 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 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* (April 15, 2020). 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. Single IRB Requirement

The DoD requires the use of a single institutional review board (IRB) in accordance with Section 219.114 of Title 32, CFR. If a DoD institution believes that the research is not subject to the provision listed in Section 219.114(b) of Title 32, CFR, the applicable DoD Component Office of Human Research Protections (COHRP) may determine and document, in accordance with Section 219.114(b)(2)(ii) of Title 32, CFR, that use of a single IRB is not appropriate for the particular context of the proposed research. Studies already in progress before January 20, 2020, will not be required to transition to a single IRB, nor submit exception documentation.

3. 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).

4. 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 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.

5. Special Requirements for IRB Review of DoD Research

5.1 Training Requirements

DoD requires that key investigators complete human research protections training. There might be specific DoD educational requirements or certification required by different DoD components. Key investigators are defined as "persons leading the performance of research".

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.

5.2 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.

5.3 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.

5.4 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.

5.5 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).

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

6.1 Prohibited Research

- Research with detainees or prisoners of war, except research with investigational new drugs or devices when the purpose is for diagnosis or treatment of a medical condition in a patient, with their informed consent, and 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.

6.2 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.

6.3 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.

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6.4 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, such as those:

- Encountered by Service members, law enforcement, or first responders while on duty.
- Resulting from or associated with high-risk behaviors or pursuits.
- Experienced by individuals whose medical conditions involve frequent tests or constant pain.

6.5 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.
- Research using fetal tissue must comply with US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g – 289g-2.

For research intending to include prisoners as participants:

In addition to allowable categories of research on prisoners identified in Subpart C, two additional categories are permissible:

- Epidemiological research that meets the waiver criteria in accordance with Pages 36929-36931 of Volume 68, Federal Register, may be approved in accordance with the applicable requirements of Subpart C of Part 46 of Title 45, CFR, DoD requirements, and other applicable requirements.
- Human subjects research that would otherwise meet exemption criteria may be conducted, but must first be approved by an IRB and must meet the requirements in Subpart C of Part 46 of Title 45, CFR, DoD requirements, and other applicable requirements.

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 IRBin accordance with Subpart C of 45 CFR 46, , the principal investigator must promptly notify the IRB. For DoD-supported research, the non-DoD institution must notify the HRPO and other federal agencies, if required.

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.

6.6 Informed Consent Element Requirements

Consent documents must include additional DoD elements of disclosure:

- 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.

7. DoD Affiliated Personnel as Research Subjects

7.1 DoD Affiliated Personnel

- DoD Affiliated Personnel means service members, reserve service members, National Guard members, DoD civilians, and DoD contractors. Service members and all Reserve Component and National Guard members in a federal duty status are considered for purposes of this issuance, to be adults. If a service member, reserve component or National Guard member in federal duty status, student at a Service Academy, or trainee is under 18 years of age, the IRB must carefully consider the research recruitment process and the necessity of including such member as a human subject.

- If the research involves DoD-affiliated personnel as subjects and if the research includes any risks to their fitness for duty (e.g. health, availability to perform job, data breach), the informed consent document must inform DoD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.

- If the research involves DoD-affiliated personnel, the key investigator must receive command or Component approval to execute the research.

- Military and civilian supervisors, officers, and others in the chain of command are prohibited from influencing their subordinates to participate in research.

- Military and civilian supervisors, officers, and others in the chain of command must not be present at any research participant recruitment sessions or during the consent process for

DoD-affiliated personnel. Excluded supervisors or those in the chain of command may participate in separate HSR recruitment sessions, if applicable.

- For greater than minimal risk research and where recruitment is conducted in a group setting, the IRB must appoint an ombudsman person. The ombudsperson:
  - Must not have a conflict of interest with the research or be a part of the research team.
  - Must be present during the research recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB-approved script and materials, including digitally provided materials.
  - Should be available to address DoD-affiliated personnel's concerns about participation.

7.2 Limitations on Compensation

Compensation to DoD-affiliated personnel for participation in research while on duty is prohibited in accordance with Title 5, U.S.C., with particular reference to Subparts G and H, with some exceptions for purposes consistent with Section 30 of Title 24, U.S.C.

7.3 Informed Consent Requirements

In order for the IRB to approve research involving DoD-affiliated personnel as human subjects the consent documentation must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.

8. Research Involving Large Scale Genomic Data (LSGD) Collected On DoD-Affiliated Personnel

DoD-conducted or DoD-supported research involving LSGD collected on DoD-affiliated personnel, or for which research the DoD provides assistance, is subject to additional requirements.

- LSGD is data derived from genome-wide association studies; single nucleotide polymorphisms arrays; genome sequencing; transcriptomic, metagenomic, epigenomic analyses; and gene expression data; etc. Research involving LSGD may or may not also constitute human subjects research. Examples of research involving LSGD includes, but is not limited to, projects that involve generating the whole genome sequence data for more than one gene from more than 1,000 individuals, or analyzing 100 or more genetic variants in more than 1,000 individuals

- The disclosure of DoD-affiliated personnel's genomic data may pose a risk to national security; accordingly, such research requires administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de-identified data or specimens.

- All research involving LSGD collected from DoD-affiliated personnel will apply an HHS Certificate of Confidentiality pursuant to Title 42, U.S.C., and Public Law 114-255.

- Research involving LSGD collected from DoD-affiliated personnel is subject to DoD Component security review to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of de-identified data or specimens

9. Additional Protections for Privacy and Confidentiality in Research

9.1 Certificate of Confidentiality (CoC)

A DoD institution conducting human subjects research or non-DoD institution conducting human subjects research with DoD support may request a CoC pursuant to Section 241 of Title 42, U.S.C. All studies involving LSGD collected on DoD-affiliated personnel (described above in section 7) will apply an HHS CoC.

- A CoC prohibits disclosing or providing, in any federal, State, or local civil, criminal, administrative, legislative, or other proceeding, or to any other person not connected with the research, the name of any individual or any such information, document, or biospecimen that contains identifiable information about the individual, created or compiled for purposes of research.

- Exceptions to the CoC must be listed in all informed consent documents, pursuant to this issuance and as stated in Section 241 of Title 42, U.S.C

10. Other DoD-Specific Requirements

10.1 Reporting Requirements

The following must be promptly reported to the HRPO (generally within 30 days of the event):

- IRB-approved changes to research that involve changes to key investigators or institutions; decreased benefit or increased risk to subjects in greater than minimal risk research as defined in Part 219 of Title 32; addition of vulnerable populations, or DoD-affiliated personnel as subjects.

- Transfer of research oversight to a different IRB.

- Notification by any federal body, State agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that the non-DoD institution's DoD-supported research is under investigation.

- Any unanticipated problems involving risks to subjects or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DoD-supported research.

- The results of the IRB's continuing review, if required.

- Change in status when a previously enrolled human subject becomes pregnant, or when the researcher learns that a previously enrolled human subject is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with Subpart B of 45 CFR 46.

- Change in status when a previously enrolled human subject becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with Subpart C of 45 CFR 46.

- A DoD-supported study's closure.

10.2 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.

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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.