

Guidance: Additional Requirements for Department of Defense (DoD) Sponsored Research.

The information included in this guidance has been adapted, with permission, from the University of Michigan's guidance on DoD Sponsored Research.

> **Introduction**

Research sponsored by the Department of Defense (DoD) involving collaboration with the DoD, involving DoD facilities, or involving DoD personnel (military or civilian), is subject to additional requirements (32 CFR 219) 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. Each DoD Component (e.g., Army, Navy, Air Force) may have additional requirements beyond those in this guidance document, therefore investigators are encouraged to check with their sponsoring Research Program Manager about any additional requirements. It is the investigators responsibility to review these requirements and plan accordingly. The MUSC IRB will not alter the established deadlines for institutional review as a result of the investigator not planning appropriately to accommodate these requirements.

> **When must Human Subject Research comply with DoD Special Requirements?**

Human subject research must comply with DoD requirements when:

- The research is funded by a DoD Component, including cases where MUSC 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 Affiliated Personnel include 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 guidance, to be adults.

- 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.

> **Single IRB Requirement and Multi-Site/Collaborative Research**

The DoD requires the use of a single IRB in accordance with 32 CFR 219.114. If an Investigator believes that the research is not subject to the provision listed in 32 CFR 219.114(b), the applicable DoD Component Office of Human Research Protections (COHRP) may determine and document, in accordance with 32 CFR 219.114(b)(2)(ii) use of a single IRB is not appropriate for the context of the proposed research.

Any DoD institutions collaborating in human subjects research with non-DoD institutions may rely on the collaborating non-DoD institution's IRB if **all of** the following conditions are met:

- Each institution engaged in non-exempt human participant research must have a current federal assurance of compliance; and
- The non-DoD institution's IRB is registered in accordance with Subpart E of Part 46 of Title 45, CFR; and
- The DoD institution reviews the protocol to ensure all applicable local and DoD requirements are addressed in the protocol; and
- The DoD institution, non-DoD institution, and the non-DoD institution's IRB have a written agreement defining the responsibilities and authorities of each institution in complying with all legal requirements. The agreement must specify that the non-DoD IRB will apply the DoD requirements specified in DoDI 3216.02, including but not limited to non-DoD institutional responsibilities defined under DoDI 3216.02 section 3.6(b); and
- If the research constitutes classified human participant research, the COHRP must approve the agreement to rely on the non-DoD institution's IRB.
 - All allegations related to classified human subjects research must be reported immediately.

> **IRB Review**

When an IRB at a non-DoD institution reviews DoD-supported research, the IRB must consider the scientific merit of the research.

The following information should be included in the MUSC eIRB application and/or research protocol:

1. The purpose of the research should be explained in an understandable and transparent manner and include the significance of the research question and the scientific approach.

2. Description of the research procedures and where the research will take place.

3. Documentation that all investigators and study team members engaged in the conduct of human subject research have completed and up to date MUSC CITI Human Subject Research: Biomedical Investigators and Key Personnel basic course or Social and Behavioral Investigator and Key Personnel basic course. The Good Clinical Practice and ICH course is also required.

- The DoD Component may evaluate MUSC's training program and records to ensure that personnel are qualified to perform the research, based upon the complexity and risk of the research. Additional DoD educational requirements or certifications may be required by different DoD components. Investigators should contact the Program Officer at the DoD/DoD Component regarding additional training or educational requirements.

- It is the PI's responsibility to ensure that research staff has completed all appropriate educational requirements as mandated by DoD policy.

4. Description of the procedures for recruitment of DoD Affiliated Personnel (if applicable)

- If a service member, reserve component or National Guard member in federal duty status, a 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 a member as a human subject.

- Military and civilian supervisors, officers, and others in the chain of command are prohibited from influencing their subordinates to participate in research and 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 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 (advocate) person. The ombudsperson must:

- o Not have a conflict of interest with the research or be a part of the research team;

- o 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; and

- o Be available to address DoD-affiliated personnel's concerns about participation.

5. If the research involves the use of surveys/interviews, explain if DoD affiliated personnel (military or civilian) or their families will complete the surveys/interviews as part of the research.

- If a survey crosses DoD Components, additional review and approval is required by the DoD and documentation of this review must be provided to the MUSC IRB.

6. If the research is conducted outside of the United States (International Research), the PI must confirm that:

- Permission to conduct the research in that country was obtained by certification or local ethics review; and

- All local laws, national laws, regulations, customs, and practices have been met and are being followed.

- o Cultural sensitivities in the setting where the research will take place should be considered.

- o

7. Describe any potential risks:

- for the revocation of clearance, credentials, or other privileged access or duty; and/or

- to the fitness for duty (e.g. health, availability to perform the job, data breach)

- **NOTE:** 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:

- o 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
-

8. Explain participant compensation and include the amount, schedule, and method of payment

- 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.
- The following limitations on dual compensation for U.S. military personnel apply for DoD funded research:
 - An individual may not receive pay from more than one position for more than 40 hours of work in one calendar week. This limitation on dual compensation includes temporary, part-time and intermittent appointments.
- Individuals may receive compensation for research activities if the research activities take place outside of scheduled work hours.
- Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to \$50 for each blood draw.
- Non-Federal persons may be compensated for research participation other than blood draws in a reasonable amount approved by the IRB according to local prevailing rates and the nature of the research.

9. Description of how privacy and confidentiality will be protected

- Data or information acquired by the DoD component under a pledge of confidentiality for exclusively statistical purposes must be used exclusively for statistical purposes and may not be disclosed in identifiable form for any other purpose, except with the informed consent of the respondent
- A DoD institution conducting human subjects research or non-DoD institution conducting human subjects research with DoD support may request a Certificate of Confidentiality (CoC) pursuant to Section 241 of Title 42, U.S.C.

- 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
- List any exceptions to the CoC pursuant to this guidance and as stated in Section 241 of Title 42, U.S.C.

10. DoD should be listed as the funding source

When necessary, the IRB may rely on outside experts to provide an evaluation of scientific merit. At MUSC, each department chairman or center director is ultimately responsible for the review and scientific integrity of any proposal that is sent to the MUSC IRB.

> **Informed Consent Requirements**

In order for the IRB to approve research involving DoD-affiliated personnel as human subjects the consent documentation must include the following additional DoD elements of disclosure:

1. A statement that the DoD or a DoD organization is funding the study
2. A statement that representatives of the DoD are authorized to review research records
3. Disclosures for research-related injury for the requirements of the DoD Component (See HRPP 4.16)
 - The DoD component may have stricter requirements for research-related injury than the Department of Health and Human Services requirements
4. Describe any potential risks for the revocation of clearance, credentials, or other privileged access or duty and/or to the fitness for duty (e.g. health, availability to perform the job, data breach) and advise the potential participant that they should seek command or Component guidance before participating.
5. List any exceptions to the CoC

> Limitations on Waivers of Informed Consent and Consent by Legally Authorized Representative (LAR)

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

- Experimental subjects are 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. 10 USC 980, as implemented by DoDI 3216.02, section 3.11

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.

An IRB may waive or alter some elements of informed consent for research involving human beings as experimental subjects, so long as it preserves the informed consent of the participant (i.e., the consent indicates that participation in the research is voluntary, and the participant/representative is informed of research risks).

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 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.

Waivers of consent are prohibited for DoD classified research.

> **Additional Requirements for Research that Involves 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:
 1. 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.
 2. 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 IRB in accordance with Subpart C of 45 CFR 46, it is the PI's responsibility to promptly notify the IRB. For DoD-supported research, the non-DoD institution must notify the HRPO and other federal agencies, if required. except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed

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

> Additional Requirements for Research Involving Large Scale Genomic Data (LSGD) Collected on DoD Affiliated Personnel

DoD-conducted or DoD-supported research involving Large Scale Genomic Data (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.

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 deidentified 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 deidentified data or specimens.

> **DoD Human Research Protection Office (HRPO) Review**

Upon completion of the MUSC IRB review and approval, the Human Research Protection Office (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 MUSC IRB and the proposed research comply with DoD requirements for the protection of research participants. The HRPO may require changes to the research before the start of the research. The Principal Investigator is responsible for submitting the information required by the sponsoring Component.

> **DoD Component Level Administrative Review (CLAR)**

The DoD Component must also conduct a Component Level Administrative Review (CLAR) of all non-exempt human subject research when any of the following conditions occur:

- Research is conducted in a foreign country, unless it is conducted by a DoD overseas institution, or involves subjects who are DoD-affiliated personnel that are U.S. citizens.
- The involvement of DoD personnel in the conduct of the research is secondary to that of the non-DoD institution.
- The research requires a waiver of informed consent pursuant to Paragraph (b) of Section 980 of Title 10, U.S.C.
- The research is fetal research as described in Sections 289g–289g-2 of Title 42, U.S.C.
- Large Scale Genomic Data (LSGD) is collected from DoD-affiliated personnel. LSDG includes data derived from genome-wide association studies; single nucleotide polymorphisms arrays; genome sequencing; transcriptomic, metagenomic, epigenomic analyses; and gene expression data; etc.
- The research constitutes classified human subject research as defined in DoDI 326.02 section 3.13.
- Research is required to be approved by the DoD Office for Human Research Protections.
- Component review includes review of reliance agreements.

> **Prohibited Research**

1. 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.”

2. Human testing of chemical or biological agents, except for certain prophylactic, protective, or peaceful purposes. Before any expected testing of chemical or biological agents involving human participant research can begin, the DoD component seeking to conduct such research must obtain explicit written approval from the DoD Office for Human Research Protections (DOHRP).

> **Reporting Requirements**

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

- IRB-approved significant 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
 - the 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 being audited or is under investigation for cause.
-

- 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

> **Recordkeeping**

Consistent with MUSC IRB policy, research records must be maintained for at least 6 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 MUSC. 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.

References:

1. [DOD INSTRUCTION 3216.02](#)
2. [dod_guidance.pdf](#)
3. [Johns Hopkins Medicine - Department of Defense \(DoD\) Requirements for the Conduct of Human Subjects Research](#)