25.11 Research supported by the Department of Defense (DoD)

Research supported by the Department of Defense (DoD) is reviewed and conducted in compliance with part 219 of title 32 CFR, part 980 of title 10 USC, applicable parts of title 21 CFR (50, 56, 312, 600, 812), DoD Instruction 3216.02, DoD Directive 3210.07, and applicable additional requirements from respective DoD component(s).
DoD Components refers collectively to the organizational entities within the DoD that are subject to the human subjects protections laid out in Department of Defense Directive

A. Application and Scope

The following additional requirements apply to all biomedical and social/behavioral research involving human research participants conducted under the jurisdiction of University of Virginia when it:

- Conducts, reviews, approves, oversees, supports manages otherwise is contractually subject to regulation by the DoD; and/or
- Human subject research performed under the jurisdiction of University of Virginia using DoD property, facilities, or assets.

In most cases, protocols covered by these requirements also will have review, approval and oversight by the DoD Human Research Protections Program.

University of Virginia assures that DoD supported research complies with all relevant DoD human subjects protection requirements, including but not limited to:

- The Belmont Report
- Title 32 Code of Federal Regulations Part 219 (32 CFR 219), Department of Defense Regulations, “Protection of Human Subjects” (DoD adoption of the “Common Rule”)
- Title 45 Code of Federal Regulations Part 46, (45 CFR 46) Department of Health and Human Services Regulations, “Protection of Human Subjects,” Subparts B, C, and D as made applicable by DoD Directive (DoDD) 3216.02
- Title 21 Code of Federal Regulations 50, 56, 312, and 812, Food and Drug Administration (FDA) Regulations
- DoDD 3216.02, “Protection of Human Subjects and Adherence to Ethical Standards in DoD-supported Research”
- Title 10 United States Code Section 980 (10 USC 980), “Limitation on Use of Humans as Experimental Subjects”
- DoDD 3210.7, “Research Integrity and Misconduct”
- DoDD 6200.2, “Use of Investigational New Drugs in Force Health Protection”

B. Key Additional Requirements Not Covered by Title 45 CFR 46, Subparts B, C and D; 21 CFR 50, 56, 312, and 812

1. Minimal Risk – [DoDI 316.02, enclosure 3, para 6b]

The definition of minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests" shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their 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.)

2. Undue Influence – [DoDD 3216.2, enclosure 3, para 7e1]

Service members shall follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty and for approving off-duty employment or activities. Superiors (e.g., military and civilian supervisors, unit officers, and noncommissioned officers (NCOs)) are prohibited from influencing the decisions of their subordinates (e.g., junior enlisted personnel and equivalent civilians) regarding participation as subjects in research involving human subjects. Unit officers and senior NCOs in the chain of command shall not be present at the time of research subject solicitation and consent during any research recruitment sessions in which members of units under their command are afforded the opportunity to participate as research subjects. When applicable, officers and NCOs so excluded shall be afforded the opportunity to participate as research subjects in a separate recruitment session. During recruitment briefings to a unit where a percentage of the unit is being recruited to participate as a group, an ombudsman not connected in any way with the proposed research or the unit shall be present to monitor that the voluntary nature of individual participants is adequately stressed and that the information provided about the research is adequate and accurate.

3. Education and Training – [DoDD 3216.2, enclosure 3, para 5]

For initial and continuing research ethics education for all personnel who conduct, review, approve, oversee, support, or manage human participant research is required. The DoD component may evaluate the education policies to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.

4. Appointment of a Research Monitor – [DoDI 3216.02, enclosure 3, para 8]

- The IRB considers the appointment of a research monitor:
    - Required for research involving greater than minimal risk, although the IRB or organizational official can require this for a portion of the research or studies involving no more than minimal risk if appropriate.
    - The research monitor is appointed by name and shall be independent of the team conducting the research.

- There may be more than one research monitor (e.g. if different skills or experience are needed.
- The monitor may be an ombudsman or a member of the data safety monitoring board.
- The IRB staff shall communicate with research monitors to confirm their duties, authorities, and responsibilities.
- The duties of the research monitor are determined on the basis of specific risks or concerns about the research.
    - May perform oversight functions (e.g. observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis).
    - May discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study.
    - Report observations and findings to the IRB or a designated official.

- The research monitor has the authority to:
    - Stop a research study in progress.
    - Remove individuals from study.
    - Take any steps to protect the safety and well-being of participants until the IRB can assess.

5. ***Additional protections for pregnant women, prisoners, and children (Subparts B, C and D) of 45 CFR 46) – [DoDI 3216.02, enclosure 3 para 7]***

- Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C. and D.
    - For purposes of applying Subpart B, the phrase "biomedical knowledge" shall be 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 included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.
    - Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.
    - The exemption for 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.
    - Research involving a detainee as a human participants is prohibited.
- Research involving prisoners cannot be reviewed by the expedited procedure.
- When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.

- In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:
    - The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.
    - The research presents no more than minimal risk
    - The research presents no more than an inconvenience to the participant.
- When a prisoner becomes a participant, if the researcher 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 organizational official and DoD Component office review the IRB's approval to change the research protocol. Otherwise, the IRB Chair shall require that all research interactions and interventions with the prisoner-subject (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 human participant has become a prisoner, shall promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, 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 involving human participants 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.

6. ***Limitation of Waivers and Exceptions from Informed Consent - [DoDI 3216.02, enclosure 3 para 13; 10 U.S.C. 980]***

The requirements of title 10 United States Code 980 which are applicable to DoD sponsored research must be considered. 10 USC 980 requires that "Funds appropriated to the Department of Defense may not be used for research involving a human being as an Experimental Subject unless 1) the informed consent of the subject is obtained in advance; or 20 in the case of research intended to be beneficial to the subject, the informed consent may be obtained from a legal representative of the subject.

The definition of experimental subject is found in DODI 3216.02 and has a much narrower definition than human subject under 45CFR46. Research with experimental subjects must involve an intervention or interaction where the primary purpose of the research is to collect data regarding the effects of the intervention or interaction.

An individual not legally competent to provide informed consent (e.g. , incapacitated individuals, cognitively impaired, minors) may not be enrolled as an experimental subject in a DOD –supported experiment unless participation in the research is intended to benefit each subject enrolled in the study, to include subjects enrolled in study placebo arms. Studies designed in a manner that permits all subjects to potentially benefit directly from medical treatment or enhanced surveillance beyond the standard of care can meet the 10 USC 980 requirements.

10 USC 980 is only applicable to certain intervention studies. It does not apply to retrospective studies, observational studies, blood draws, and tissue collections.

If the research participant meets the definition of "experimental subject," policies and procedure prohibit a waiver of the consent process unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering. The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met:

- The research is necessarily to advance the development of a medical product for the Military Services.
- The research may directly benefit the individual experimental subject.
- The research is conducted in compliance with all other applicable laws and regulations.

For classified research, waivers of consent are prohibited.

7. ***Limitations on Compensation for U.S. Military Personnel - [Dual Compensation Act and 24 U.S.C. 30]***

The Dual Compensation Act prohibits an individual from receiving pay from more than one position for more than an aggregate of 40 hours of work in one calendar week. This prohibition applies to employees paid from either appropriated or non-appropriated funds, or a combination thereof, and includes temporary, part-time and intermittent appointments. This law if not applicable to enlisted off-duty military personnel in relation to their military duty.

When research involves U.S. military personnel, limitations on dual compensation include:

- 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, as approved by the IRB according to local prevailing rates and the nature of the research.
- Prohibit an individual from receiving pay of compensation for research during duty hours.
- U.S. military personnel may be compensated for research if the participant is involved in the research when not on duty.

8. ***Requirement for Reporting - DoDI 3216.02, enclosure 3 para 4(b)(4)***

The Institution shall promptly (no longer than within 30 days) notify the HRPO of the following: when significant changes to the research protocol are approved by the IRB, the results of the IRB continuing review, if the IRB used to review and approve the research changes to a different IRB, when the institution is notified by any Federal department or agency or national organization that any part of its HRPP is under investigation for cause involving a DoD-supported research protocol, and all UPIRTSOs, suspensions, terminations, and serious or continuing noncompliance regarding DoD-supported research involving human subjects.

9. ***Recordkeeping Requirements - [DoDD 3216.2, para. 5.3.2; SECNAVINST 3900.39D, para. 8c(18)]***

Recordkeeping requirements for DOD-supported research with human subjects are longer than the Common Rule's requirement. DOD may require submitting records to DOD for archiving.

Records maintained that document compliance or non-compliance with DoD requirements shall be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

10. ***Addressing and Reporting Allegations of Non-Compliance with Human Research Protections - [DoDD 3216.2, para. 4.10; SECNAVINST 3900.39D, para. 8d(2) and 6k]***

Report the initiation of all investigations and report results regardless of the findings to the Navy Secretary General and appropriate sponsors.

11. ***Addressing and Reporting Allegations of Research Misconduct - [DoDD 3216.2, para. 4.8; DODD 3210.7; SECNAVINST 3900.39D, 8d(2) para. 6l]***

All findings of serious research misconduct under this section shall be reported to the Director, Defense Research and Engineering.

12. Provisions for Research with Human Subjects using Investigational Test Articles (Drugs, Device and Biologics) - [DoDD 3216.2, para 4.9; DoDD 6200.2; SECNAVINST 3900.39D, para. 6h]

Principal investigators may not be sponsors for INDs and IDEs.

13. ***Prohibition of Research with Prisoners of War (POW) and Detainees - [DoDD 3216.2, para 4.4.2; SECNAVINST 3900.39D, para. 6a(8)]***

Research involving any person captured, detained, held or otherwise under the control of DoD personnel (military and civilian, or contractor employee) is prohibited.

14. ***Classified research[DoDI 3216.02, enclosure 3 para 13]***

The involvement of classified information may be limited to information needed for IRB approval and oversight of the research; information needed to inform the human subjects during the consent process; and information provided by the human subjects during the course of the research. Secretary of Defense approval is required for all classified non-exempt research involving human subjects.

Informed consent procedures shall include:
(1) Identification of the Department of Defense as the supporting institution of the research, 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.
(2) A statement that the research involving human subjects is classified and an explanation of the impact of the classification.

The IRB shall determine whether potential human subjects need access to classified information to make a valid, informed consent decision.

IRB review shall be conducted using a full board review. Use of an expedited review procedure is prohibited.

15. Additional Requirements for DoD Sponsored Research

a) New research and substantive scientific amendments to approved research shall undergo scientific review and the review is considered by the IRB. The IRB may rely on outside experts to provide an evaluation of scientific merit.
b) When conducting research with international populations, additional safeguards for research conducted with international populations include: The Organization or Researcher has permission to conduct research in that country by certification or local ethics review and the Researcher follows all local laws, regulations, customs, and practices.
c) Disclosure regarding the provisions for research-related injury follow the requirements of the DoD component.
d) Surveys performed on Department of Defense personnel must be submitted, reviewed, and approved by the Department of Defense after the research protocol is reviewed and approved by the IRB.
e) When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.
f) The following shall be promptly (no longer than within 30 days) reported to the DoD human research protection officer:
    a. When significant changes to the research protocol are approved by the IRB.
    b. The results of the IRB continuing review.
    c. Change of reviewing IRB.

d. When the organization is notified by any Federal department, agency or national organization that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol.

g) If consent is to be obtained from the research participant's LAR, the research must intend to benefit the individual participant. The determination that research is intended to be beneficial to the individual research participant must be made by the IRB.

C. Responsibilities

It is the responsibility of the principal investigator to ensure compliance with all additional Department of Defense (DoD) requirements for human subject protection. It also is the responsibility of the IRB to ensure that all additional requirements by Department of Defense components for human subject protection have been met before IRB approval of the research project.