UNLV Office of RESEARCH INTEGRITY RESEARCH PROTECTIONS

Guidance - Department of Defense Requirements

General Description

Research that is regulated by federal agencies often times have agency-specific requirements. This guidance is the assist researchers and the IRB in identifying additional regulatory considerations.

When it applies / context

This guidance may be used by members of the UNLV Human Research Protection Program (HRPP), Researchers and the IRB. Researchers should review this guidance when conducting research supported by the Department of Defense (DoD). The IRB should use this guidance to review for agency-specific requirements in research supported by the DoD.

Considerations & Best Practices

Definitions-As Defined in Department of Defense Instruction (DoDI) 3216.02, November 8, 2011

Minimal Risk

- The definition of the minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests" must not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. See DoDI 3216.02 for more specific details of applicability.
- 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).

Experimental Subject

- The definition of research involving a human being as an experimental subject is an activity, for research purposes, where there is an 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 experiment subject is a subset of research involving human subjects.
- If the research participant does not meet the definition of "experimental subject," the IRB may waive the consent process.
- If the research participant meets the definition of "experimental subject," a waiver of the consent process is prohibited unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering. The Assistant Secretary for Defense for Research and Engineering may waive the requirements for consent when all of the following are met:
    - The research is necessary 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.

Education

For all personnel who conduct, review, approve, oversee, support, or manage human participants research, initial and continuing research ethics education is required. IRB or EC staff, chair, and members; and Researchers and Research Staff are responsible to become aware of the specific requirements contained in DoD regulations and requirements and educated themselves about these requirements when appropriate.

Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.

Multi-site Research
The UNLV IRB does not serve as the reviewing IRB for DoD-covered research studies.

IRB Considerations

During the review, the IRB should consider the following when evaluating the appointment for a research monitor:

- Required for research involve 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 must 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 must approve a written summary of the monitors' duties, authorities, and responsibilities.
- The IRB or HRPP official must 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.

For non-exempt research, the IRB must consider the scientific merit of the research. The IRB may rely on outside experts to provide an evaluation of the scientific merit.

The IRB must make a determination regarding the following, as appropriate:

- The disclosure for research-related injury follow the requirements of the DoD component
- If research is intended to be beneficial to the individual experimental subject
    - If consent is to be obtained from the experimental subjects' legal representative, the research must intend to benefit the individual participant.

Additional consent requirements for DoD research:

- A statement that the DoD or a DoD organization is funding the study.
- A statement that representatives of the DoD are authorized to review research records.

Waivers

- For classified research, waivers of consent are prohibited.
- When conducting emergency medicine research, the PI must obtain approval from the DOHRP on behalf of the Secretary of Defense for a waiver of the advance informed consent provisions of 10 USC 980. The PI will provide the waiver documentation to the IRB.

Additional Safeguards for Participants

For research conducted with international populations,

- The Researcher has permission to conduct research in that country by certification or local ethics review.
- The Researcher follows all local laws, regulations, customs, and practices.

When research involves U.S. military personnel, additional protections for military research participants to minimize undue influence include:

- Officers are not permitted to influence the decision of their subordinates.
- Officers and senior non-commissioned officers may not be present at the time of recruitment
- Officers and senior non-commissioned officers have a separate opportunity to participate.
- When recruitment involves a percentage of a unit, an independent ombudsman is present.
- There are limitations on dual compensation, including:
    - Prohibit an individual from receiving pay of compensation for research during duty hours.
    - An individual may be compensated for research if the participant is involved in the research when not on duty.
    - 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 participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

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" must 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.

- Research Involving Prisoners (Subpart C)
    - 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 participant becomes a prisoner, 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 must 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, must 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.
- Research involving a detainee as a human participants is prohibited. However, this prohibition does not apply to research involving investigational drugs and devices when the same products would be offered to US military personnel in the same location for the same condition.
- Research involving prisoners of war is prohibited. The IRB is aware of the definition of "prisoner of war" for the DoD component granting the addendum.

- Research Involving Children (Subpart D),
  - 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 Experimental Subjects
  - Is conducted in accordance with 10 USC 980 as implemented by DODI 3216.03, section 3.11. Research sponsored or funded by the DoD will be reviewed under an additional set of regulations [32 CFR 219].
  - ORI-RP staff screen and review IRB application materials to identify DoD-related research
  - ORI-RP staff establish and document collaborative agreements with other institutions and individuals engaged in DoD-related research
  - ORI-RP staff contact the PI, if necessary, to obtain missing information, or documents to complete application

- Research involving greater than minimal risk involving DoD-personnel
  When recruitment and consent occurs in a group setting, the IRB must appoint an ombudsperson. The ombudsperson must not have a conflict of interest with the research or be a part of the research team, they must be present during human participant 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 provide materials. They should be available to address DoD-affiliated personnel's concerns about participation.

- Research involving large scale genomic data collected on/from DoD-affiliated personnel will apply a DHHS Certificate of Confidentiality.
- If the research involves DoD-affiliated personnel as participants, in addition to the basic and required consent disclosures, consent documents must include:
    - If the research involves risks to their fitness for duty (e.g., health, availability to perform job, data breach), the informed consent document (ICD) must inform DoD- affiliated personnel about these risks and that they should seek command or component guidance before participating.
    - If applicable, a statement of potential risks for the revocation of clearance, credentials, or other privileged access or duty.
    - A statement that the DoD or a DoD organization is funding the study.
    - A statement that representatives of the DoD are authorized to review research records.
- For greater than minimal risk research, consent documents must include the disclosure that participants may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility, and this eligibility for health care services extends beyond participants' participation in the study to such time after the study has ended.
    - Written materials must document how organizations will care for participants with research-related injuries, including injuries that are the direct result of activities performed by DoD-affiliated personnel in studies that are collaborative with a non-DoD institution.
- If the research involves a human being as an experimental subject and is supported by DoD-appropriated funds, informed consent must be obtained from the participant in advance, in accordance with 10 USC 980.
    - If the participant is unable to provide informed consent and consent will be obtained in advance from the participant's

legal representative, the research must be intended to benefit the individual participants.

- If non-exempt research is supported by DoD-appropriated funds and involves experimental subjects as defined in DODI 3216.02, consent must be obtained in advance in accordance with DODI 3216.02, consent must be obtained in advance in accordance with 10 USC980
    - The IRB may waive or alter some elements of informed consent for researching 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.
    - If consent is to be obtained from the legal representative of the experimental subjects as defined in DODI 3216.02, the research must intend to benefit each participant enrolled in the study.

- Fetal research:
    - Research or experimentation may not be conducted, in the United States or in any other country, on a nonviable living human fetus ex utero or a living human fetus ex utero for whom viability has not been ascertained unless the research or experimentation:

      May enhance the well-being or meet the health needs of the fetus or enhance the probability of its survival to viability; or

      Will pose no added risk of suffering, injury, or death to the fetus and the purpose of the research or experimentation is the development of important biomedical knowledge which cannot be obtained by other means.

    - The risk standard must be the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term.
    - For human participant research that would not otherwise be approved but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, written approval from the DOHRP must be obtained through the COHPR prior to research starting.
    - Human participant research involving prisoners that would otherwise meet exemption criteria may be conducted, but must first be approved by an IRB/EC and meet the requirements of Subpart C and DoDI 3216.02.

- DoD organizations conducting research involving prisoners must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with Subpart C.
- When a previously enrolled human participant becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with Subpart C, the researcher must promptly notify the IRB.
    - For DoD-conducted research, the human protections director must notify the COHRP.
    - For DoD-supported research, the non-DoD organization must notify the DOHRP and other federal agencies.
    - The DOHRP must concur with the IRB before the participant can continue to participate while a prisoner.
- Service members and DoD-affiliated personnel are considered to be vulnerable to coercion and undue influence by the DoD due to the nature of the command structure of the organization.
  Therefore, additional protections for DoD-affiliated personnel are required, as follows (DoDI 3216.02 section 3.9 (f)):
    - If the research involves DoD-affiliated personnel as participants 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 researcher 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 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.
    - Service members and all Reserve component and National Guard members in a federal duty status are considered 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 HSR recruitment process

and the necessity of including such member as a human participant.

- In order to approve research involving DoD-affiliated personnel, the IRB or component HRPO must determine whether the following requirements have been satisfied:
  - The consent documentation must include, if applicable, potential risks for revocation of clearance, credentials, or other privileged access or duty.
  - For research involving recruitment of DoD-affiliated personnel in research determined to be greater than minimal risk, and when recruitment occurs in a group setting, the IRB/EC must appoint an ombudsperson. 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 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.
- Compensation to DoD-affiliated personnel for participation in research while on duty is prohibited in accordance with 5 USC, with particular reference to Subparts G and H, with some exceptions for purposes consistent with 24 USC 30.

- Research involving large-scale genomic data from DoD-affiliated personnel is subject to additional requirements:
  - The disclosure of DoD-affiliated personnel's genomic data may pose a risk to national security; accordingly, written materials must describe administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de-identified data or specimens.
  - All research involving large-scale genomic data collected from DoD-affiliated personnel must have a Certificate of Confidentiality from DHHS (Title 42, U.S.C., and Public Law 114-255).
  - Research involving large-scale genomic data 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.

- Human participant research involving the testing of chemical or biological agents is prohibited, pursuant to Section 1520a of Title 50, United States Code (U.S.C.). Some exceptions for research for prophylactic, protective, or other peaceful purposes apply. Before any excepted 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).

  Chemical agents (a chemical substance that is intended for use in military operations to kill, seriously injure, or incapacitate a person through its physiological effects. Excluded form consideration are riot control agents, chemical herbicides, smoke, and flame). (Section 1520A of Title 50, United Code (U.S.C)).

  Biological agents means any microorganism (including bacteria, viruses, fungi, rickettsia, or protozoa), a pathogen or infections substance and any naturally occurring, bioengineered or

synthesized component of any such micro-organism, pathogen, or infectious substance, whatever its origin or method of production, that is capable of causing death, disease or other biological malfunction in a human, an animal, a plant, or another living organism; or deterioration of food, water, equipment, supplies, or materials of any kind; or deleterious alteration of the environment (DoD Directive 5210.65)

Required DoD Human Research Protections Office (HRPO) Administrative Review

Upon completion of UNLV 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 UNLV and the proposed research comply with DoD requirements for the protection of research participants. While the HRPO review is not an IRB review, 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.

Required DoD Component Level Administrative Review (CLAR)
The DoD Component must also conduct a CLAR of all non-exempt HSR 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 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.

The research constitutes classified HSR.

Research is required to be approved by the DoD Office for Human Research Protections.

Surveys and 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 UNLV's 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 the Component review must be provided to the IRB.

Other Considerations

Non-exempt classified research must also be conducted following the requirements of Instruction 3216.02.

The following must be promptly (no longer than within 30 days) reported to COHRP (DoDI 3216.02 section 3.6) by the Principal Investigator:

- When significant changes to the research protocol are approved by the IRB.
- The results of the IRB continuing review.
- Changes to key investigators or institutions
- Change of reviewing IRB.
- When UNLV is notified by any federal department, agency, or national organization that any part of an HRPP is under investigation for cause involving a DoD-supported research protocol.
- Any determinations of serious or continuing non-compliance of DoD-supported research
- Any unanticipated problems involving risks to participants or others for any DoD-supported

research

- Audits by federal or state agency, official governing body of a Native American or Alaskan native tribe, other official entity or foreign government
- Allegations of serious or continuing noncompliance related to research involving human participants that are substantiated by investigation, and subsequent actions taken based on the findings
- Substantiated allegations related to classified HSR must reported immediately
- Any suspension or termination of DoD-supported research
- Addition of vulnerable populations as participants
- Change in status when previously enrolled participant becomes pregnant, or when the researcher learns that a previously enrolled participant is pregnant and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46, Subpart B.
- Change in status when a previously enrolled participant becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with 32 CFR 219, Subpart C

Records maintained that document compliance or non-compliance with DoD regulations must 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.

Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD after the research protocol is reviewed and approved by the IRB. When a survey crosses DoD components, additional review is required. When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.

Resources

Instruction 3216.02 p.13 http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf

Instruction 3216.03 Department of Defense Instruction Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research

32 CFR 219

Section 980 of Title 10, United States Code (U.S.C.)

Section 1520a of Title 50 United States Code (U.S.C.)

AAHRPP Elements: I.1.A., I.1.E., I.1.F., I.3., I.5.D., II.2.D., II.2.E., II.2.F., II.2.G., II.2.H., II.3.A., II.3.B., II.3.C., II.3.F., II.3.G., II.4.A., II.4.B., II.4.C., II.5.A., II.5.B., III.1.E., III.1.F., III.2.D.