1. PURPOSE

1.1. This guidance outlines the additional obligations of investigators conducting research supported or conducted by Department of Defense (DOD).

2. GUIDANCE

2.1. Training and education

2.1.1. All personnel who conduct, review, approve, oversee, support, or manage human subjects research are required to undergo initial and continuing research ethics education.

2.1.2. There may be specific DOD educational requirements or certification required.

2.1.3. DOD may evaluate the organization's education policies to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.

2.1.4. As the investigator, you must be aware of the specific requirements contained in DOD regulations and requirements and educated about these requirements when appropriate.

2.2. Scientific Review

2.2.1. The IRB must consider the scientific merit of the research.

2.2.2. The IRB may rely on outside experts to provide an evaluation of the scientific merit.

2.3. International Research

2.3.1. You or the organization must obtain permission to conduct research in that country by certification or local ethics review.

2.3.2. You must follow all local laws, regulations, customs, and practices.

2.4. DOD Component Administrative Review, Approval and Oversight.

2.4.1.1. The DOD Component must conduct an administrative review (also known as a component-level administrative review (component-level administrative review)) of all non-exempt human subject research when any of the following conditions occur:

2.4.1.1.1. Human subject research is conducted in a foreign country, unless conducted by a DOD overseas institution, or only involves DOD-affiliated personnel who are U.S. citizens.

2.4.1.1.2. The research requires a waiver of informed consent pursuant to 10 USC 980, Subsection B

2.4.1.1.3. Large-scale genomic data (LSGD) is collected from DOD-affiliated personnel. LSGD includes data derived from genome-wide association studies; single nucleotide polymorphisms arrays; genome sequencing; transcriptomic, metagenomic, epigenomic analysis; and gene expression data; etc. (See definition in Department of Defense Instruction (DODI) 3216.02

2.4.1.1.4. The research constitutes classified research involving human subjects (DODI 3216.02 section 3.13).

2.4.1.1.5. Research is required to be approved by the Directorate of Human Subjects Protection (DOHRP), in addition to the Component Office of Human Research Protections (COHRP), in accordance with DODI 3216.02

2.4.1.1.6. Component review includes review of reliance agreements.

2.5. Reporting: The following findings in DOD-supported research must be reported to the DOD human research protection officer within 30 days:

2.5.1. Determinations of <Serious Noncompliance> or <Continuing Noncompliance>
2.5.2. Significant changes to the research protocol that are approved by the IRB
2.5.3. The results of the IRB continuing review
2.5.4. Change of reviewing IRB
2.5.5. When the organization is notified by any Federal department, agency or national organization that any part of an HRPP is under investigation for cause requirements
2.5.6. Closure of a DoD-supported study
2.5.7. <Unanticipated Problems Involving Risk to Subjects or Others>
2.5.8. <Suspension of IRB approval>
2.5.9. <Termination of IRB approval>
2.5.10. Change in status when a previously enrolled subject becomes pregnant, or when the investigator learns that a previously enrolled subject is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46, Subpart B.
2.5.11. Change in status when a previously enrolled subject becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with 32 CFR 219, Subpart C

2.6. Survey Approval

2.6.1. Surveys performed on DOD personnel must be submitted, reviewed, and approved by the DOD after the research protocol is approved by the IRB.

2.7. Multisite Research

2.7.1. When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.

2.8. Definition of <Minimal Risk>

2.8.1. 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. 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).
2.8.2. The organization applies this definition to all research regardless of funding.

2.9. Appointment of an Ombudsperson for greater than minimal risk research when recruitment and consent occurs in a group setting. The ombudsperson:

2.9.1. Must not have a conflict of interest with the research or be part of the research team
2.9.2. Must be present during human subject 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.
2.9.3. Should be available to address DoD-affiliated personnel’s concerns about participation.

2.10. 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 and may not be disclosed in identifiable form for any other purpose, except with the informed consent of the respondent.

2.10.1. All studies involving large scale genomic data collected on/from DOD-affiliated personnel will apply a Department of Health and Human Services (DHHS) Certificate of Confidentiality.

2.11. Research involving large-scale genomic data from DoD-affiliated personnel is subject to additional requirements:

2.11.1.1. 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.

2.11.1.2. 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).

2.11.1.3. 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.

2.12. Recruitment of Service Members

2.12.1.1. Officers are not permitted to influence the decision of their subordinates.

2.12.1.2. Officers and senior non-commissioned officers may not be present at the time of recruitment.

2.12.1.3. Officers and senior non-commissioned officers have a separate opportunity to participate.

2.12.1.4. When recruitment involves a percentage of a unit, an independent ombudsman is present.

2.12.1.5. 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)):

2.12.1.5.1. 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

2.12.1.5.2. 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 subject.

2.12.2. Compensation of Service Members:

2.12.2.1. Service member may not receive pay or compensation for research during duty hours.

2.12.2.2. A service member may be compensated for research if the subject is involved in the research when not on duty.

2.12.2.3. Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw.

2.12.2.4. Non-Federal persons may be compensated for participating in research involving other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

2.13. Consent

2.13.1. The disclosure for research-related injury must follow the requirements of the DOD component.

2.13.2. If the subject undergoes interactions or interventions for research purposes, the subject is considered an “experimental subject.” For experimental subjects:

2.13.2.1. A waiver of the consent process is prohibited unless a waiver is obtained from the Assistant Secretary of DOD for Research and Engineering.

2.13.2.2. The Assistant Secretary for DOD for Research and Engineering may waive the requirements for consent when all of the following are met:

2.13.2.2.1. The research is necessary to advance the development of a medical product for the Military Services.

2.13.2.2.2. The research may directly benefit the individual experimental subject.

2.13.2.2.3. The research is conducted in compliance with all other applicable laws and regulations.

2.13.2.3. The IRB may waive the consent process for subjects who are not “experimental subjects.”

2.13.2.4. If consent is to be obtained from the experimental subjects’ legal representative, the research must intend to benefit the individual subject.

2.13.2.4.1. The determination that research is intended to be beneficial to the individual experimental subject must be made by an IRB.

2.13.3. Waivers of consent are prohibited for classified research.

2.13.4. If the research involves DOD-affiliated personnel as subjects, in addition to the basic and required consent disclosures, consent documents must include:

2.13.4.1. 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.

2.13.4.2. If applicable, a statement of potential risks for the revocation of clearance, credentials, or other privileged access or duty.

2.13.5. For greater than minimal risk research, consent documents must include the disclosure that subjects 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 subjects’ participation in the study to such time after the study has ended.

2.13.5.1. Written material must document how AdventHealth will care for subjects 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.

2.14. 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 10 USC 980:

2.14.1. 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 subject (i.e., the consent indicates that participation in the research is voluntary and the subject/representative is informed of research risks).

2.15. Chemical or Biological Warfare Agents

2.15.1. Research involving chemical or biological warfare agents, including research for prophylactic, protective, or other peaceful purposes involving chemical or biological agents is prohibited at AdventHealth.

2.16. Research on Pregnant Women

2.16.1. Research involving pregnant women and fetuses as subjects is subject to HHS Subpart B except:

2.16.1.1. The phrase “biomedical knowledge” is replaced with “generalizable knowledge.”

2.16.1.2. The applicability of Subpart B is limited to research involving pregnant women as subjects 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 subjects.

2.17. Research on Prisoners

2.17.1. Research involving prisoners is subject to HHS Subparts C.

2.17.2. Research involving prisoners cannot be reviewed by the expedited procedure.

2.17.3. When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.

2.17.4. In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:

2.17.4.1. The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.

2.17.4.2. The research presents no more than minimal risk.

2.17.4.3. The research presents no more than an inconvenience to the subject.

2.17.5. When a subject becomes a prisoner, if the investigator asserts to the IRB that it is in the best interest of the prisoner-subject to continue to participate in the research while a prisoner, the IRB chair may determine that the prisoner-subject may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the institutional 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 subject 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-

subject can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-subject's confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human subjects from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-subject to continue to participate in the research. This approval is limited to the individual prisoner-subject and does not allow recruitment of prisoners as subjects.

2.17.6. Research involving a detainee as a human subjects is prohibited.

2.17.6.1. 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.

2.17.7. Research involving prisoners of war is prohibited.

2.17.7.1. "Prisoner of war" includes any person captured, detained, held, or otherwise under the control of DOD personnel (military, civilian, or contractor employee). Such persons include: Enemy Combatant, Lawful Enemy Combatant, Unlawful Enemy Combatant, Enemy Prisoner of War, Retained Person, and Civilian Internee. Such persons do not include personnel of the DOD being held for law enforcement purposes. It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power.

2.17.7.2. This prohibition does not apply to activities covered by investigational new drug or investigational device provisions for the purpose of diagnosis or treatment of a medical condition in a patient. Such treatment (e.g., an investigational new drug) may be offered to detainees with the detainees' informed consent when the medical products are subject to FDA regulations for investigational new drugs or investigational medical devices, and only when the same product would be offered to members of the U.S. Military Services in the same location for the same medical condition and only when consistent with established medical practice involving investigational drugs and devices.

2.17.8. In addition to the categories of permissible human subject research involving prisoners identified in DHHS regulations Subpart C, additional categories are permissible:

2.17.8.1. Human subject research involving prisoners that would otherwise meet exemption criteria may be conducted, but must first be approved by an IRB and meet the requirements of Subpart C and DODI 3216.02.

2.17.9. When a previously enrolled human subject becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with Subpart C, the investigator must promptly notifify the IRB

2.17.9.1. For DOD conducted research, the human protections director must notify the COHRP

2.17.9.2. For DOD-supported research, the non-DOD organization must notify the DOHRP and other federal agencies

2.17.9.3. The DOHRP must concur with the IRB before the subject can continue to participate while a prisoner

2.18. Research on Children

2.18.1. Research involving children is subject to the HHS Subpart D.

2.18.2. 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.

2.19. Research on Fetal Tissue

2.19.1. Fetal research must comply with US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

2.19.2. 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:

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

2.19.2.2. 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.

2.19.3. 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.

2.19.4. For human subject 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 COHRP prior to research starting.

2.20. Waiver of Informed consent for Planned Emergency Research

2.20.1. An exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of DOD.

2.21. Records

2.21.1. Records maintained that document compliance or <Noncompliance> 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.

2.22. Non-exempt Classified Research

2.22.1. 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 subjects during the course of the research.

2.22.2. Secretary of DOD approval is required for all classified non-exempt research involving subjects.

2.22.2.1. Submission for approval must be from the Head of the OSD or DOD Component conducting or supporting the non-exempt research involving human subjects. The request must be coordinated with the ASD(R&E) and General Counsel of the Department of DOD after the oIRB has approved the research.

2.22.3. Waivers of informed consent are prohibited.

2.22.4. Informed consent procedures must include:

2.22.4.1. Identification of the DOD as the supporting institution of the research, unless the research involves no more than minimal risk. The Secretary of DOD may grant an exception to this requirement on the grounds that providing this information could compromise intelligence sources or methods.

2.22.4.2. A statement that the research involving human subjects is classified and an explanation of the impact of the classification.

2.22.5. IRB approval process must meet the following requirements:

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

2.22.5.2. At least one non-affiliated member must be a non-Federal employee (other than as an individual appointed as an expert or consultant for purposes of service on the IRB).

2.22.5.3. Any IRB member who disagrees with a majority decision approving a project may appeal the decision to the Secretary of DOD. The appeal must be included in the DOD Component's submission to the Secretary of DOD.

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

2.22.6. Disclosure or use of classified information must comply with DOD requirements for access to and protection of classified information.

3. REFERENCES

3.1. 10 USC 980
3.2. DOD Instruction 3216.02
3.3. DOD Instruction 3216.2
3.4. OPNAVINST 5300.8B
3.5. SECNAVINST 3900.39D