DEPARTMENT OF DEFENSE GUIDE FOR RESEARCHERS AT THE UNIVERSITY OF IOWA

Institutional Review Board and Human Subjects Office

Table of Contents

Department of Defense Guide for Researchers

1. Introduction

The information in this Guide is intended for University of Iowa (UI) investigators engaged in research involving human subjects and that is supported by, or is in collaboration with, the U.S. Department of Defense (DoD). The information presented here applies to all biomedical and social/behavior human subjects research involved with a DoD component.

Research activities which include "both a systematic investigation designed to develop or contribute to generalizable knowledge AND involve a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable private information" will hereinafter be referred to as "research involving human subjects." *(DoD Instruction, Glossary - DoD-supported research involving human subjects)*

Research with the DoD may involve duties and obligations in addition to those required by the UI IRB. Each component of the DoD may also have specific requirements for the application review process. The responsibility for upholding these requirements is shared among researchers, the IRB/HSO, the UI, and the DoD.

Please see Appendix I for a list of DoD components and Appendix II for a list of selected laws and regulations applicable to DoD-supported research. In this document, 'DoD Instruction' refers to DoD Instruction 3216.02, April 15, 2020, and specifically to Section 3 thereof unless otherwise noted.

This Guide is intended only as a general reference. It is important to check with the DoD contact for specific details or with questions about the particular study.

2. What Is Department of Defense Research?

Research involves the DoD when:

- The research is funded by a DoD component, or
- The research involves cooperation, collaboration, or other type of agreement with a component of the DoD or its personnel, or
- The research uses DoD resources, including its equipment, property, facilities, assets, personnel, or identifiable data or specimens from living individuals, or
- The subject population will intentionally include personnel (military and/or civilian) from a component of the DoD. *(DoD Instruction, Glossary - DoD-supported Research Involving Human Subjects)*

DoD policies do not apply when US military personnel incidentally participate as subjects in a study that is not DoD-supported and US military personnel are not the intended target population.

3. Planning a Project with the DoD

Researchers should expect and plan for additional costs, actions, and documentation that may be associated with DoD-supported research. For example, when a scientific reviewer is required,

costs for the reviewer should be included when developing the application. Consider the following when planning to do research with the DoD:

Requirements for Additional Training

The DoD requires training in human subjects research. In addition to the CITI course required by the UI, the Navy requires additional certification modules offered through the CITI program. For directions on how to access these modules for existing CITI users, go here ***Chris, please link to DoD Existing CITI Users doc saved in 2.2.0.4***. Direction on accessing these modules for new CITI users can be found here ***Chris, please link to DoD New CITI Users doc saved in 2.2.0.4***

Check with the DoD representative to determine if other training is needed or if current training should be recertified. Rules and regulations specific to the Navy and the Marines may be found in SECNAVINST 3900.39D.

Scientific Review

The Army and Navy require independent scientific review and approval of nonexempt research prior to IRB review of new applications and substantive modifications. The review may be conducted by the funding agency (including the DoD), through the use of an established internal review mechanism in the PI's school or department, or via an ad hoc scientific review by the researcher's chair or dean.

When scientific review is required, the PI must provide documentation to the IRB upon submission of the initial IRB application or substantive amendments. Scientific review must demonstrate that the research uses procedures consistent with sound research design and is likely to yield the expected results and should include an assessment of the following:

- Significance of the research question;
- Scientific approach;
- Research team qualifications;
- Facilities and resources available; and
- Adequate subject protections.

The name and qualifications of the reviewer(s) should be included as part of the review.

At the UI, the requirement for scientific review will be met by the Departmental Executive Officer's (DEO's) signature on the Assurance submitted by the PI as part of the IRB submission. The form for documenting scientific review is incorporated with the Assurances.

Approval of Surveys

Research involving surveys or interviews with DoD military or civilian personnel or their families may require DoD approval. Check with the DoD contact to determine if there are additional requirements and whether the approval is required before or after IRB review.

Navy Research and IND/IDEs
Investigators doing research with the Navy may not be designated as sponsors of an Investigational New Drug (IND) or Investigational Device Exemptions (IDE). Only the Surgeon General, Commanders, and Commanding Officers may be sponsors. *(SECNAVINST 3900.39D(6)(h). Research Involving the Use of Investigational Test Articles.)*

4. Required Review by the DoD Human Research Protection Office or Other DoD Component

After the completed IRB review and approval, the application must be submitted to the applicable DoD Human Research Protection Office (HRPO) for administrative review by the Principal Investigator. The HRPO may require changes to the research. Research must not begin before this review is completed. In the event changes are required by the HRPO, a modification must be submitted to the IRB for review and approval. A copy of the HRPO correspondence should be attached to the modification. Additionally, a DoD component-level administrative review (CLAR) must be conducted when:

- The research requires a waiver of informed consent pursuant to 10 USC 980, Subsection (b).
- The research is fetal research, as described in 42 USC 289g-289g-2.
- 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 analyses; and gene expression data; etc. (See definition in DoDI 3216.02 G.2 Definitions)
- The research is required to be approved by the DOHRP (in addition to the COHRP) in accordance with DoDI 3216.02.

The Principal Investigator is responsible for ensuring all DoD related reviews are completed prior to the commencement of the research activities.

5. International Research

According to 32 CFR § 219.101, research involving non-U.S. citizens may be conducted outside the United States. However, in the conduct of such research, the laws, customs, and practices of the country in which the research is conducted or those required by this regulation, whichever are more stringent, will take precedence. The research must meet the same standards of ethics and safety that apply to research conducted within the United States involving U.S. citizens and will be conducted in accordance with applicable international agreements.

The PI is responsible for determining whether the sponsoring DoD component requires an additional ethics review by the host country or a local DoD IRB with host country representation. The Navy requires that international research involving human subjects who are not U.S. citizens or DoD personnel, conducted outside the United States, its territories and possessions, requires permission of the host country. The laws, customs, and practices of the host country and those required by the instruction will be followed. An ethics review by the host country, or local Naval IRB with host country representation, is required. *(SECNAVINST 3900.39D (6)(i). International Research.)*

6. Collaboration

Collaborating institutions in multi-site research must have a federalwide assurance. Investigators must provide documentation of IRB approval or an IRB Authorization Agreement for collaborators. The roles and responsibilities of each institution must be specified in any such Agreement, along with a statement by which the parties agree to comply with any special DoD requirements.

7. Force Health Protection

Force Health Protection is the healthcare program designed to meet the actual, anticipated, or potential needs of military personnel in relation to military missions. When using an IND under a force health protection program, the DoD Components involved in implementation shall provide prior notice to personnel receiving the drug or biological product and provide all pertinent clinical information to health care providers who administer the IND. *(DoD Instruction 6200.02, February 27, 2008, E4.7 Training and Risk Communication)*

8. Prohibited Research

Certain types of research are prohibited by the DoD and/or the UI:

- Research with *detainees* (prisoners of war), except research with investigational new drugs or devices 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. As described in DoD Directive 2310.01E, a detainee is "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."

  The UI, by policy, allows classified research under certain conditions as outlined in the University of Iowa Policy manual 27.2(b).
- Research involving human subjects for testing of chemical or biological warfare agents is generally prohibited, except for certain prophylactic, protective or peaceful purposes. *(50 USC §1520a(b))*

9. Unique Limitations on Waivers of Informed Consent

Generally, an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent under 32 CFR §§ 219.116 (c) and (d). These are also the conditions under which an IRB may waive consent for DoD-conducted and DoD-supported research involving human subjects.

Research Involving a Human Being as an Experimental Subject is an activity for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction. *(DoD Instruction, Glossary)*

The definition of research involving a human subject as an experimental subject is a subset of but is not the same as the definition of research involving human subjects. When the research meets the Glossary definition of research involving a human being as an experimental subject, informed consent must be obtained in advance from the experimental subject or the subject's legal

representative consistent with 32 CFR § 219 if the subject cannot consent. If consent is to be obtained from the experimental subject's legal representative, the IRB must have first determined that, consistent with 32 C.F.R. part 219, the research is intended to benefit the individual subject. *(DoD Instruction, 9.b. Unique Limitations on Waiver of Informed Consent)*

The requirement of paragraph 9.b. of DoD Instruction may be waived by the Assistant Secretary of Defense for Research and Engineering (ASD(R&E)) if all the following conditions are met:

(1) The research is necessary to advance the development of a medical product for the Military Services.
(2) The research may directly benefit the individual experimental subject.
(3) The research is conducted in compliance with all other applicable laws and regulations.

10. Vulnerable Populations

The DoD requires that pregnant women/fetuses/neonates, prisoners, and children have the protections of the Common Rule subparts B, C, and D. *(45 CFR. part 46)* There are also protections for the cognitively impaired, those with mental illness or physical disabilities, or other circumstances that may require special protection.

DoD Requirements Involving Pregnant Women
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.

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 DAF Component Office of Human Research Protections (COHPR) prior to research starting.

DoD Requirements When a Subject Becomes Incarcerated
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/EC.

- For DoD-supported research, the non-DoD organization must notify the DOHRP and other federal agencies.
- The DOHRP must concur with the IRB/EC before the participant can continue to participate while a prisoner.

In addition to the vulnerable populations with which researchers may be familiar, the Navy also includes severely ill patients, employer/employee, student/teacher, supervisor/subordinate, and deployed personnel as among the groups that may require additional protection. *(SECNAVINST 3900.39D November 6, 2006 – 6. Policy (a)(6) Vulnerability and Additional Protections)*

11. Enrolling Adult Subjects Who Cannot Provide Consent

For research involving a human being as an experimental subject:

a. Informed consent must be obtained from the subject or subject's Legally Authorized Representative (LAR). If consent is to be obtained from a LAR, the IRB must have first determined that, consistent with 32 C.F.R. part 219, the research is intended to benefit the individual subject. *(DoD Instruction, 9.c. Unique DoD Limitations on Waiver of Informed Consent)*

12. Inclusion of Subject Populations

The IRB understands that the selection of human subjects must reflect gender and minority participation in DoD-conducted or supported clinical research involving human subjects and shall comply with Public Law 103-160, Section 252 – Inclusion of Women and Minorities in Clinical Research Projects. The requirement to include women and minorities may be waived by the Secretary of Defense if the Secretary determines that the project is 1) inappropriate with respect to the health of the subjects, 2) is inappropriate with respect to the purpose of the research, or 3) is inappropriate under such other circumstances as the Secretary of Defense may designate.

13. Minimal Risk

Risk is minimal where the probability and magnitude of physical or psychological harm is that which is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. *(45 CFR § 46.303(d))*

When evaluating risk for DoD-supported research, "the phrase 'ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests' in the definition of minimal risk 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)." *(DoD Instruction, 6.b. Selection of Human Subjects and Evaluating Risk, Evaluating Risk)*

14. Protections from Medical Expenses

The Common Rule does not require payment or reimbursement of medical expenses, provision of medical care, or compensation for research-related injuries. For studies that involve more than minimal risk, informed consent requires an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained. *(32 CFR § 219.116(a)(6)).* Every Navy research project involving greater than minimal risk shall include an arrangement for emergency treatment and necessary follow-up of any research-related injury. (SECNAVINST 3900.39D(6)(a)(5)). The IRB application for Navy projects must specify (a) whether any compensation is available if injury occurs and (b) a plan for emergency treatment and necessary follow-up of any research related injury.

15. Military Participants

Adult Status. The age of majority in Iowa is eighteen. *(Iowa Code § 599.1)* For the purpose of participating in DoD-supported or conducted research, active duty service members and reserve

component members are considered to be adults. If a subject is an active duty service member or reserve component member in a federal duty status, that person is considered for purposes of this Guide to be an adult, even if the person is under eighteen. *(DoD Instruction, 12. Service Members and Their Status as Adults)*

Command Approval. Military personnel may need command approval before participating in human subjects research because some research may impact readiness in the field. As part of the IRB review, investigators will be asked to provide documentation of command approval. The UI IRB requires that the documentation be in the form of an attached letter of agreement, indicating that the PI\team has permission to conduct research at the location.

Protecting Service Members from Undue Influence. Care must be taken to assure that officers and senior non-commissioned officers do not influence the decision of subordinates to participate in human subjects research and are not present during recruiting. In addition, if recruiting superior officers, they must be recruited in a separate session from their subordinates. The HawkIRB application documents military status of research team members who will obtain consent in order for the IRB to assess this requirement. Additional protections for DoD-affiliated personnel are required, as follows (DoDI 3216.02 section 3.9 (f)). In order to approve research involving DoD-affiliated personnel, the IRB or component HRPO must determine whether the following requirement has been satisfied:

- The consent documentation must include
  - potential risks for revocation of clearance, credentials, or other privileged access or fitness for duty(e.g., health, availability to perform job, data breach) and that they should seek command or component guidance before participating in the research.
  - A statement that the DoD or DoD organization is funding the research
  - A statement that representatives of the DoD are authorized to review research records

For research that has been determined by the IRB to be more than minimal risk and where recruiting is conducted in a group setting, an ombudsman must be present to ensure that information is clearly, accurately and adequately presented and that the voluntary nature of participation is emphasized. *(DoD Instruction 7.e. DoD Personnel as Subjects (1) Military Personnel as Subjects, (a), (b), (c), and (d).)*

16. DoD Civilian Personnel

DoD civilian personnel that are recruited for research have the same protections as military personnel (#15 above). The requirement for an ombudsman is at the discretion of the IRB.

17. Limits on Compensation

The DoD has very specific requirements regarding compensation paid to DoD employees, whether they are active duty military or DoD civilian employees *(DoD Instruction, 11. Compensation to Human Subjects for Participation in Research)*. Investigators who plan to compensate subjects may need to ask subjects about their military status in order to comply with

the requirements below. Investigators should describe their plan for this assessment of military status in the IRB application.
The current compensation plan is as follows:

On-duty federal personnel including military members:

- Up to $50 for blood draws
- Compensation is not allowed for general research participation

Off-duty federal personnel including military members:

- Up to $50 for blood draws
- Compensation is allowed for general research participation, as approved by the IRB. Payment may not come directly from a federal source. Payment from a federal contractor or non-federal source is permissible.

Non-federal personnel:

- Up to $50 for blood draws
- Compensation is allowed for general research participation, as approved by the IRB. Payment may come from a federal or non-federal source.

18. Reporting

The IRB and the PI are required to report certain events to the HRPO. The following occurrences involving a DoD-supported research protocol must be reported to the DoD within 30 days of the event:

- Determinations of serious or continuing noncompliance
- Unanticipated problems involving risks to subjects or others
- Study suspensions or terminations
- Audits, inspections or investigations
- Results of the IRB Continuing Review
- Changes to the reviewing IRB
- Substantive amendments to the protocol that are approved by the IRB. Amendments must be reviewed and approved by the HRPO prior to implementing the change to the study.

(DoD Instruction, 4.b.(4). Research Involving Human Subjects Conducted by a Non-DoD Institution, Non-DoD Institutional Responsibilities)

19. Recordkeeping

Generally, research records should be kept for the length of time required by UI or federal policy, usually 3-6 years after the completion of the research. However, individual DoD components may have additional requirements, including the transfer of records to the DoD component. There should also be a research record retained at UI unless there is an executable data usage agreement specifying otherwise. Retained records shall be made accessible for inspections and copying by authorized representatives of the DoD.

Appendices

Appendix I

Selective List of DoD Components

Components are entities within the DoD - the Office of the Secretary of Defense, the Military Departments, the Office of the Chairman of the Joint Chiefs of Staff and the Joint Staff, the Combatant Commands, the Office of the Inspector General of the Department of Defense, the Defense Agencies, the DoD Field Activities, and all other organizational entities within the DoD. Components include:

- Air Force
- Air Force Academy
- Army
- Army Corps of Engineers
- Coast Guard
- Coast Guard Academy
- Defense Advanced Research Projects Agency (DARPA)
- Defense Intelligence Agency
- Marines
- Military Academy (West Point)
- Missile Defense Agency
- National Geospatial-Intelligence Agency
- National Guard
- National Security Agency
- National War College
- Naval Academy
- Navy
- Office of Naval Research
- Pentagon Force Protection Agency
- Tricare Health System
- U.S. Naval Observatory

Appendix II

Selected List of Applicable Laws, Regulations, and Policies

UI DoD/Navy Addendum

DoD/DoN Addendum to FWA expires 6/14/27.

DoD Regulations and Guidance

32 CFR part 219, Protection of Human Subjects

DoD Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research, April 15, 2020

10 USC 980, Limitations on the Use of Humans as Experimental Subjects

Department of Defense Instruction 3210.7, Research Integrity and Misconduct

Department of Defense Instruction 6200.2, Use of Investigational New Drugs in Force Health Protection

DoD Component Requirements

Department of Defense, Office of the Secretary of Defense for Personnel and Readiness

HA Policy 05-003, Policy for Protection of Human Subjects in Department of Defense Sponsored Research

Department of the Army

Information for Investigators, June 23, 2020

AR 70---25, Use of Volunteers as Subjects of Research, January 25, 1990

AR 40---38, Clinical Investigation Program, September 1, 1989

AR 40---7, Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances, October 19, 2009

Department of the Navy

SECNAV Instruction 3900.39D, Human Research Protection Program, November 6, 2006

Department of the Navy, Training and Education Guidance

Marine Corps Survey Program

Department of the Air Force

Air Force Instruction 40---402, Protection of Human Subjects in Research

This is not an authoritative list of all regulations or guidance that may apply to DoD-supported human subjects research. Check with the DoD contact for more information.

Acknowledgment

The Human Subjects Office gratefully acknowledges the University of Michigan Office of Research for permission to use much of the information produced in this Guide.