



OFFICE OF RESEARCH SUBJECT PROTECTION GUIDANCE

Human Subjects Research Supported by the Department of Defense

Human-subjects research that is supported by the Department of Defense (DoD) or one of its components (e.g., Departments of the Army, Air Force, and Navy and Marine Corps) through a contract, grant, cooperative agreement, or other arrangement must comply with DoD Regulations for “Protection of Human Subjects” at 32 CFR 219 and with DoD Directive 3216.2. Other DoD component-specific requirements may also apply depending on the study.

This guidance is intended to highlight some of the primary issues for investigators to be aware of when conducting DoD-supported research, but is not a substitute for investigators to obtain project-specific information about DoD’s requirements from the applicable DoD human research protection administrator as directed below. Investigators are expected to include information relevant to and address any applicable DoD requirements in their protocol submissions to Broad IRBs of Record.

DoD Definitions

The following definitions apply to human-subjects research supported by the DoD or one of its components:

Research means any systematic investigation, including research, development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

Research involving a human being as an experimental subject means 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.

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. The phrase "ordinarily encountered in daily life or during the performance of routine physical or psychological examinations 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 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 Directive 3216.2 Requirements

The DoD and its components have adopted the “Common Rule” Federal policy for protection of human subjects in research. DoD’s implementation of the Common Rule is found at 32 CFR 219. Additional DoD policies and requirements for the protection of human subjects are described in DoD Directive 3216.2.

Most of the DoD requirements outlined in DoD Directive 3216.2 are consistent with Broad IRB of Record policies and procedures. However, DoD has imposed certain restrictions on the use of surrogate consent and waiver of informed consent and additional human subject protections for research involving greater than minimal risk. Investigators should be aware of these and other additional requirements when developing proposals for DoD support. Some of the main additional requirements are described below.

Because components of DoD may have additional requirements for human subject protection, investigators should obtain DoD component specific requirements from the applicable DoD human research protection administrator when applying for funding.

1. Scientific Merit

The Broad IRB of Record must consider the scientific merit of non-exempt research.

2. Education and Training

DoD may impose additional education and training requirements on investigators beyond those required by the Broad IRB of Record. Investigators should contact their DoD human research protection administrator for information about specific education requirements.

3. Additional Protections for Human Subjects

DoD-supported research must meet the additional protections for pregnant women, human fetuses, neonates, prisoners and children in 45 CFR 46, Subparts B, C, and D unless modified by DoD as below:

a. Pregnant Women, Human Fetuses and Neonates as Subjects

When applying Subpart B regarding pregnant women, human fetuses and neonates, the phrase "biomedical knowledge" shall be replaced with "generalizable knowledge." The applicability of Subpart B is limited to research involving pregnant women as human subjects involved in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus or involving a fetus or neonate as human subjects. Research involving human subjects using fetal tissue must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g. When applicable, investigators are required to provide an assessment of risks and potential benefits to pregnant women and fetuses, nonviable neonates and

neonates of uncertain viability and children in the application to the Broad IRB of Record.

b. Prisoners

When applying Subpart C regarding prisoners, researchers should contact the Broad IRB of Record before submitting research involving prisoners.

When a previously enrolled subject becomes a prisoner and the researcher asserts to the Broad IRB of Record that it is in the best interest of the prisoner-subject to continue to participate in the research while a prisoner, the Broad IRB of Record 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 (IO) 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 will promptly review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. 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.

c. Detainees or Prisoners of War

Research involving a detainee as a human subject is prohibited. This prohibition does not apply to activities covered by investigational new drug or investigational device provision when for the purposes of diagnosis or treatment of a medical condition in a patient. Such treatment may be offered to detainees with the detainees' informed consent when the medical products are investigational 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.

d. Children as Subjects

When applying Subpart D to children, the exemption 45 CFR 46 101(b)(2) of research involving survey or interview procedures or observation of public behavior does not apply to research with children, except for research

involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

e. Military Personnel as Subjects

Investigators should describe the procedures for recruitment of any military personnel in the protocol submission. The recruitment plan should adhere to the following DoD requirements for selection of subjects:

If the human subject research involves DoD-affiliated personnel, the principal investigator must receive approval from the DoD-affiliated personnel's command or DoD Component to conduct the research. If the human subject research takes place on a DoD facility, the principal investigator must also receive approval from the command or DoD Component responsible for the facility.

Superiors (e.g., military, and civilian supervisors, unit officers, and noncommissioned officers (NCOs)) are prohibited from influencing the decision of their subordinates (e.g., junior enlisted personnel and equivalent civilians) regarding participation as subjects in research.

Superiors of Service members (e.g., unit officers, senior NCOs and equivalent civilians) in the chain of command must not be present at any human subject recruitment sessions or during the consent process for DoD-affiliated personnel. When applicable, superiors are excluded from these recruitment sessions and will be given the opportunity to participate in the research in a separate recruitment session.

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 recruitment process and the necessity of including such member as a human subject.

For research that involves more than minimal risk to subjects and when recruitment occurs in a group setting, the IRB will appoint an ombudsman. The ombudsman must not have a conflict of interest with the research or be part of the research team and must be present during the recruitment in order to monitor that the voluntary involvement or recruitment of the Service members is clearly and adequately stressed and that the information provided about the research is clear, adequate, and accurate. The ombudsman should be available to address DoD-affiliated personnel's concerns about participation.

f. DoD Civilians as Subjects

DoD Civilians must follow their organization's policies regarding the

requirement to obtain permission to participate in research involving human subjects. As above, supervisors are prohibited from influencing the decisions of their subordinates regarding participation in research and may not be present at any human subject recruitment sessions or during the consent process. When applicable, supervisors will be afforded the opportunity to participate as human subjects in a separate recruitment session.

4. Informed Consent

No DoD component may support research involving a human being as an experimental subject without requiring the prior informed consent of the subject with certain limited exceptions described below. Investigators should take these restrictions into consideration when describing the consent process in the protocol submission.

a. DoD-affiliated Personnel as Human Subjects

In order to approve research involving DoD-affiliated personnel as human subjects, the IRB must determine whether the consent document must include, if applicable, potential risks for the revocation of clearance, credentials or other privileged access or duty.

b. Legally Authorized Representatives

For research involving a human being as an experimental subject to which Section 980 of Title 10, U.S.C., applies, informed consent must be obtained in advance from the experimental subject or the subject's legal representative (consistent with Part 219 of Title 32, CFR, if the subject cannot consent). If consent is obtained from the subject's legal representative, the intention of the principal investigator must be for the research to be beneficial to the subject.

c. Waiver of Informed Consent

The requirement for prior informed consent may be waived by DoD officials if all of the following conditions are met:

- The research is to advance the development of a medical product necessary to the DoD;
- The research may directly benefit the individual experimental subjects; and
- The research is conducted in compliance with all other applicable laws and regulations.

Research subject to DoD requirements is prohibited from using an exception from consent in emergency medicine research unless a waiver is obtained from the Secretary of Defense.

5. Research-related Injury

All human subjects research that is determined to be greater than minimal risk must meet the requirement of Section 219.116 of Title 32, CFR, to provide subjects with an explanation as to whether any compensation and any medical treatments are available for research-related injuries.

The Broad IRBs of Record often provide templates that include the provision of care for treatment of research-related injuries. Investigators should contact their DoD human research protection administrator about any additional research-related injury requirements and communicate those to the Broad IRB of Record.

6. Compensation of Military Personnel

Compensation to DoD-affiliated personnel for participation in research while on duty is prohibited. U.S. military personnel may be compensated for research if they participate 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 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.

7. Multi-Site Research and International Research

Single IRB is required for DOD supported multi-site research subject to the 2018 Common Rule. A reliance agreement must be executed between the reviewing IRB and the relying institution, outlining each party's roles with respect to the research under review.

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

- The DoD institution determines the non-DoD institution has an appropriate federal assurance or that a federal assurance is not required.
- The non-DoD institution's IRB is registered in accordance with Subpart E of 45 CFR 46.
- The DoD institution and the non-DoD institution enter into an agreement specifying that the non-DoD IRB will apply the DoD requirements specified in DoD Instruction 3216.02.
- The DoD institution reviews the protocol to ensure all applicable local and DoD requirements are addressed in the protocol.

When the research is conducted outside the United States or its territories, and the research involves subjects who are not U.S. citizens or DoD personnel, the

investigator must obtain permission of the host country and follow Broad IRB of Record policies and procedures for research conducted outside the United States or its territories.

8. Surveys of DoD Personnel

Surveys of DoD personnel generally must be submitted to DoD for review and approval.

9. Reporting Noncompliance and Research Misconduct

a. Noncompliance

DoD must be notified of any investigations of alleged noncompliance with applicable human subject protection regulations or DoD requirements outlined in Directive 3216.2 arising in DoD-supported research and of any resulting findings. Reports of noncompliance should be coordinated with the Broad IRB of Record.

b. Research Misconduct

DoD must be notified of any allegations of research misconduct and misconduct proceedings in DoD-supported research.

10. Additional Reporting Requirements

The following findings in DoD-supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer:

- Any unanticipated problems involving risks to participants or others
- Any serious or continuing noncompliance
- Any suspension or termination of IRB approval
- When the organization is notified by any Federal department, agency or national organization, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that Broad's DoD-supported research is under investigation.

For DoD-supported research, the principal investigator must report the following within 30 days to the DoD human research protection officer:

- IRB approved changes to human subject research that involve changes to principal investigators or institutions; decreased benefit or increased risk to subjects in greater than minimal risk research, addition of vulnerable populations, or DoD-affiliated personnel as subjects
- Change in status when a previously enrolled human subject becomes pregnant, or when the researcher learns that a previously enrolled human subject is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with Subpart B of 45 CFR 46
- Change in status when a previously enrolled human subject becomes a

prisoner, and the protocol was not reviewed and approved by the IRB in accordance with Subpart C of 45 CFR Part 46

- Results of IRB continuing review, if required
- Study closure
- Change of reviewing IRB