



Research Supported by the Department of Defense

I. Purpose

To describe requirements to conduct human research supported by the U.S. Department of Defense (DoD)

II. Revisions from Previous Version

None.

III. Definitions

A *DoD Addendum* to an existing FWA is one of several methods that can be used to inform institutions (Institutional Officials and IRB chairs) of DoD research requirements that differ from the OHRP-approved FWA. The DoD Addendum may include designation of the relied-upon IRB(s) and/or an outline of requirements specific to a given DoD Component. The DoD Addendum is effective as long as the FWA is in force.

DoD Components refers collectively to the organizational entities within the DoD that are subject to the DoD Directive 3216.02. These entities include the Office of the Secretary of Defense, the Military Departments, 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.

DoD Personnel includes DoD civilian employees and members of the military services, DoD contractors, Reserve Service members, National Guard members, unit officers, and noncommissioned officers (NCOs).

Detainee is defined as any person captured, detained, held or otherwise under the control of DoD personnel (military, civilian, or contractor employee). It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power.

Human Research Protection Official is a federal employee designated by a DoD Component or institution to conduct administrative review of DoD-supported research.

Research Involving a Human Being as an Experimental Subject is a subset of human research and is defined as an activity, for research purposes, where there is an intervention or interaction with a living human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction (32 CFR 219.102(f)). This definition does not include activities that are not considered research involving human subjects, activities that meet exemption criteria, and research involving the collection or study of existing data, documents, records, or specimens from living individuals. Examples include, but are not limited to, a physical procedure, a drug, a manipulation of the participant or their environment, or the withholding of an intervention that would have been undertaken if not for the research purpose.

Large Scale Genomic Data (LSGD) are data derived from genome-wide association studies; single nucleotide polymorphisms arrays; genome sequencing; transcriptomic, metagenomic, epigenomic analyses; and gene expression data; etc. Research involving LSGD may or may not also constitute human subjects research. Examples of research involving LSGD includes but is not limited to, projects that involve generated the whole genome sequence data for more than one gene from more than 1,000 individuals, or analyzing 100 or more genetic variants in more than 1,000 individuals.

Minimal Risk as defined in 32 CFR 219 does not include the inherent occupational risks that certain subjects face in their everyday life, such as those:

1. Encountered by Service members, law enforcement, or first responders while on duty.
2. Resulting from or associated with high-risk behaviors or pursuits.
3. Experienced by individuals whose medical conditions involve frequent tests or constant pain.

Support of a study generally means the provision of at least a portion of the funding, personnel, facilities, access to or information about DoD-affiliated personnel for recruitment, or data or specimens, and all other resources. Under this definition, studies that may be wholly funded internally or by a non-DoD component, such as an agency within the Department of Health and Human Services, but focus, for example, on a health concern prevalent in military populations may still fall under DoD purview. This definition does not include DoD-conducted human subjects research, whether or not conducted in collaboration between a DoD institution and non-DoD institution.

IV. Policy

Human research supported by the DoD is subject to the Common Rule (32 CFR 219, 45 CFR 46). However, because of the DoD culture, organizational structure, and population, DoD Directive 3216.02 lays out additional requirements that also apply. These requirements are designed to address risks unique to DoD personnel that differ from civilians both in the conduct of research and in participation in research (e.g., deployment, personal conduct standards, and duty to report certain personnel actions). The procedures outlined in this SOP ensure that WCM research supported by the DoD complies with all DoD regulations governing human research.

WCM's existing Federalwide Assurance (FWA) meets the DoD requirement that the institution hold a federal assurance. The existing FWA may be augmented with a DoD Addendum to inform institutions of additional DoD requirements.

The principal investigator (PI) submits documentation of Institutional Review Board (IRB) approval, the risk level, and the expiration date of the research to the DoD Component sponsoring or supporting the study. The DoD may also request additional documentation to verify compliance with federal and DoD policies, including minutes related to review of the research, determinations that an activity is not human research, any exemption determinations, or documentation of continuing approval.

The DoD applies the provisions in 45 CFR 46, Subparts B, C, and D with modifications for the protection of vulnerable classes of research participants. Additional safeguards apply when the study involves DoD personnel (both military and civilian) or international participants. WCM does not apply DoD policies when U.S. military DoD personnel incidentally participate as participants in a study that is not DoD-sponsored or supported **and** DoD personnel are not the intended target population. Under no circumstances shall the IRB approve research involving *detainees* as defined above. WCM IRB reviews research involving the testing or use of chemical or biological agents for peaceful purposes, meeting exemption criteria as outlined in Section 1520a of Title 50, United States Code.

The subset of research involving *Human Beings as Experimental Subjects* includes limitations on the waiver of informed consent.

Research under this policy must comply with all applicable biosafety and biosecurity, for example: DoD 6055.18-M, the current editions of Centers for Disease Control and Prevention, "Biosafety in Microbiological and Biomedical Laboratories (BMBL)," and the National Institutes of Health guidelines for research involving recombinant or synthetic nucleic acid molecules.

The DoD recognizes that certain activities are excluded from the requirements outlined in DoD Instruction (DoDI) 8910.01, Volumes 1 and 2 of DoD Manual 8910.01, and DoDI 1100.13. These include public or internal information collections of facts or opinions, obtained initially or in follow-up requests, from individuals (including individuals in control groups) under treatment or clinical examination in connection with research on, or prophylaxis to prevent, a clinical disorder; direct treatment of that disorder; or the interpretation of biological analyses of body fluids, tissues, or other specimens; or the identification or classification of such specimens. There may be other exclusions.

V. Procedure

DoD Addendum

1. After a Principal Investigator (PI) submits an application to a DoD component, the Office of Sponsored Research Administration (OSRA) and/or the Joint Clinical Trials Office (JCTO) Contracts Office may receive notice from the DoD that a DoD Addendum to the existing FWA may facilitate the sponsored research agreement for a pending award. OSRA and/or JCTO staff will notify the PI and the IRB of the DoD request.
2. The Institutional Official, the IRB Chair, and the Human Research Compliance (HRC) Executive Director review and sign the DoD Addendum.
3. Once a DoD Addendum is in place, it covers all WCM DoD-sponsored research for that Component; however, various DoD Components may use other processes or have additional requirements. The PI, with assistance from the IRB, is responsible for identifying additional requirements and conveying those requirements to the IRB, as appropriate.

Exempt, Limited, or Not Human Subjects Research

1. When human research meets the criteria for exemption at 45 CFR 46.104, the PI follows standard procedures in accord with the Exempt Review SOP or Limited Review as appropriate. The WCM IRB sends a copy of the IRB Exemption letter and all protocol documents to the DoD for review and concurrence. Note, the IRB does not use exempt procedures to review DoD research involving children.
2. When the project does not meet the definition of human subjects research, the IRB Staff will follow standard procedures and send a copy of the determination letter and all protocol documents to the DoD for review and concurrence.

Expedited Human Research

1. The IRB uses expedited review procedures to review minimal risk, non-exempt human research using materials (e.g., data, documents, records, or specimens) that were previously collected for any purpose, provided the materials were not collected for the currently proposed research.

Selection of Human Subjects

1. The selection of subjects in DoD-supported human subjects research must comply with Section 252 of the National Defense Authorization Act for Fiscal Year 1994 (Public Law 103-160) with respect to gender, minority participation, and membership in the Armed Services unless waived by the DoD.

Submission of DoD Supported Research to the IRB

1. DoD requires a scientific merit review of the protocol and any substantive amendments. The PI is responsible for obtaining a comprehensive scientific merit review either from the Protocol Review and Monitoring Committee (PRMC), Clinical and Translational Science Center (CTSC), or other appropriate WCM office prior to submission of the application to the IRB or through the grant peer-review process.
2. The PI or designee completes the IRB protocol, identifies the research as supported by a DoD component (as defined in DoD Directive 3216.02), and submits it to the IRB.
3. The PI is responsible for ensuring the appropriate DoD-relevant items are included in the IRB protocol. The PI should also indicate in the protocol whether DoD personnel are participants.
4. IRB staff advise the PI and the IRB of DoD-specific requirements as outlined in this SOP and the DoD Reviewer Checklist. The PI is responsible for communicating with the DoD to identify DoD component requirements specified in the grant application guidelines and advising the IRB of the requirements.
5. The PI and project team are responsible for completing processes specified in the DoD Addendum or DoD guidelines and submitting documentation, as appropriate, to the IRB as an attachment to the IRB submission.
6. In addition to the standard WCM mandatory education requirements, the PI is responsible for identifying specific educational or certification requirements of the sponsoring DoD Component and conveying those requirements to the IRB. The PI consults the DoD Component, as appropriate, to identify education requirements. Training requirements for DoD research hold a three-year expiration. Note, individual DoD components may have stricter training requirements.
7. Any DoD Component may assure that data or information acquired by the DoD Component is 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, except with informed consent. The WCM IRB may request a Certificate of Confidentiality.

Required for Greater than Minimal Risk Studies

1. The PI must include a statement that subjects may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility. This eligibility extends beyond the subjects' participation in the study to such a time after the study has ended. Subjects injured may obtain care for such injuries at a DoD medical treatment facility on a space-available basis during the pendency of the research study.
2. The PI must document how the institution will care for subjects with research-related injuries, including those that are the direct result of activity performed by DoD-affiliated personnel in studies that are collaborative with a non-DoD institution.

Research Involving U.S. DoD Personnel as Research Participants

1. If the research includes any risks to fitness for duty (e.g. health, availability to perform job, data breach), the informed consent document must inform DoD personnel about these risks and that they should seek command or Component guidance before participating.
2. The PI must receive command or Component approval to execute the research.
3. Service members and all Reserve Component and National Guard members are considered to be adults. If a potential participant 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.
4. The consent documentation must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.
5. In conducting the review, the IRB takes into consideration the unique risks involved in enrolling DoD personnel as research participants. If the IRB does not have the relevant expertise, the IRB obtains consultation from an ad hoc expert with working knowledge of the risks or from the DoD component.
6. The PI submits a participant recruitment plan (can be part of the protocol) to the IRB that incorporates additional safeguards to minimize undue influence from superiors in the chain of command, officers, and senior or other NCOs and that these individuals cannot be present at the time of recruitment or consent of their subordinates. The PI provides a separate opportunity or recruitment session for supervisors, officers, and senior NCOs to participate in the research. The PI consults the sponsoring DoD Component, as necessary, for assistance.
7. For greater than minimal risk studies involving military service members in which recruitment occurs in a group setting, the IRB must appoint an ombudsperson to be present during the recruitment and informed consent process to monitor the voluntary nature of participation and ensure that information provided is adequate and accurate. The ombudsperson must not have a conflict of interest with the research or be part of the research team and should be available to address DoD-affiliated personnel's concerns about participation.

Research Involving Pregnant Women, Fetuses, and Neonates

1. The phrase "biomedical knowledge" in Subpart B of 45 CFR 46 must be replaced with "generalizable knowledge."
2. The applicability of Subpart B of 45 CFR 46 is limited to research involving pregnant women as human subjects involved in human subjects research that is greater than minimal risk, and includes interventions, as defined in Part 219 of 32 CFR, or invasive procedures involving:
 - a. A woman or the fetus; or
 - b. fetuses or neonates as human subjects
3. Using fetal tissue must comply with Sections 289g-289g-2 of Title 42, U.S.C.

Research Involving Prisoners

1. In addition to Subpart C of 45 CFR 46, two additional categories are permissible:
 - a. Epidemiological research that meets the waiver criteria in accordance with Pages 36929-36931 of Volume 68, Federal Register, may be approved.
 - b. Human subjects research that would otherwise meet exemption criteria may be conducted after WCM IRB approval.
2. When a previously enrolled human research subject becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with Subpart C of 45 CFR 46, the researcher must promptly notify the IRB. The IRB must notify the Human Research Protection Official (HRPO) and other federal agencies, if required.

Research Involving Large-Scale Genomic Data (LSGD)

1. To disclose DoD-affiliated personnel genomic data may pose a risk to national security; accordingly, the research requires administrative, technical, and physical safeguards commensurate with risk, including secondary use or sharing of de-identified data or specimens and is subject to DoD Component security review to ensure the above.
2. All studies involving LSGD collected on DoD-affiliated personnel will apply a Certificate of Confidentiality (CoC).

Compensation for Participation in Research

1. The IRB reviews the proposed participant compensation plan to ensure that the PI is aware of DoD policies and limitations depending on whether or not participation occurs during on-duty or off-duty status and whether funds used to compensate participants come from a Federal source as follows:
 - a. DoD personnel (active duty and civilian):
 - On Duty: compensation limited to blood draws
 - May participate in research during work or duty hours with supervisor approval and no compensation other than \$50 per blood draw
 - Compensation can be from Federal or non-Federal source
 - Off Duty: No restrictions as long as the source of compensation is not Federal dollars, but compensation for up to \$50 per blood draw can be from a Federal source
 - b. Non DoD personnel:
 - No restrictions and compensation can be from a Federal or non-Federal source.

Waiver of Informed Consent

1. If the research is minimal risk, the IRB may use criteria in (45 CFR 46.116 or 32 CFR 219.116) to approve a waiver of some elements of informed consent so long as the consent preserves voluntariness and research risk information.
2. If the research meets the definition of “research involving a human beings as experimental subjects” (as defined in DoD Directive 3216.02), the PI obtains consent from the participant or the participant’s legal authorized representative (LAR).
3. The IRB makes the determination as to whether the research meets the definition of “research involving human beings as experimental subjects.” The IRB shall not approve a waiver of consent if the research includes participants meeting the definition of “research involving a human being as an experimental subject” unless the DoD has issued a waiver.
4. If consent will potentially be obtained from the participant’s LAR the IRB ensures that the research is intended to be beneficial to the experimental participants.

Multi-Site or Collaborative Research Requirements

1. Use of a single IRB (sIRB) is required unless a DoD Institution believes that the research is not subject to this provision and the applicable DoD Component Office of Human Research Protections (COHRP) determines and documents that use of a single IRB is not appropriate for the particular context of the proposed human subjects research. Studies approved before January 20, 2020 will not be required to transition to a single IRB, nor submit exception documentation.
2. For collaborative research involving WCM and DoD researchers, procedures will follow sIRB procedures. WCM and the collaborating institution will sign an IRB Authorization Agreement (IAA) which specifies the roles and responsibilities of the relying institution and the IRB of record.
3. The PI will provide the WCM IRB additional information to ensure ongoing communication among participating IRBs and sites.

DoD Supported Research Conducted Outside of the United States

1. Federal and DoD regulatory requirements and host nation laws are applicable.
2. Host nation HSR laws are not typically applicable to DoD-conducted research that only involves DoD-affiliated personnel as research subjects.
3. In cases when a DoD-affiliated person who is also a citizen of the host nation is a research subject, however, it is more likely that the host nation’s HSR laws will be applicable. DoD Components conducting and

supporting HSR outside of the United States will consult with legal counsel, on a case-by-case basis, to determine whether host nation HSR laws are applicable. Where differences in applicable standards exist, the standard that is most protective of human subjects will be applied.

4. The PI must provide written notification to the U.S. Central, U.S. Africa, U.S. European, U.S. Indo-Pacific, and U.S. Southern Commands of human subjects research that is to be conducted or supported in their area of responsibility before human subjects research proceeds. This does not apply at DoD institutions overseas.

Additional DoD Review Required Prior to Initiation of Study

1. After the IRB completes its review and issues approval, documentation is submitted to the DoD Component sponsoring or supporting the study, including:
 - i. Documentation that the research has been reviewed and approved by the IRB, including risk level, expiration date, scientific merit, amendments, and additional reviews;
 - ii. Documentation of key investigators' human research protection training; and
 - iii. IRB approved protocol documents, including FWA and IRB registration numbers.
2. The DoD may also request additional documentation of initial and ongoing to verify compliance with federal and DoD policies, including minutes related to the research. As appropriate, IRB staff will provide the PI any additional information pertinent to IRB review, which may not be under a PI's purview. The PI sends requested information to the DoD.
3. The PI may not initiate the study until the human research protection officer (HRPO) within the sponsoring DoD Component reviews and approves the IRB approval and other submitted documentation.
4. The PI notifies OSRA and/or JCTO and IRB staff upon receipt of relevant HRPO authorization and/or DoD Survey Review approval, as appropriate. OSRA staff release the award only after receiving certification of final human research and survey review and approval from the HRPO or relevant DoD designee.

Reporting and Recordkeeping

1. The PI will promptly (within 30 days) notify the DoD HRPO of:
 - a. IRB approval of changes to the research protocol, including changes to key 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;
 - b. Transfer of human research oversight to a different IRB;
 - c. Notification by any federal body, State agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that the non-DoD institution's DoD-supported human research is under investigation;
 - d. Results of IRB continuing review;
 - e. Participant complaints;
 - f. Unanticipated problems involving risks to participants or others;
 - g. Instances of serious or continuing noncompliance;
 - h. Study closure;
 - i. Suspension or termination of IRB approval; 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 45 CFR 46 Subpart B;
 - j. 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 45 CFR 46 Subpart C;
 - k. A DoD-supported study's closure; and
 - l. Any Federal department or agency or national organization for cause investigation involving a DoD-supported human research protocol.
2. IRB staff will make records accessible for inspection by authorized representatives of the DoD and/or supporting DoD Component. Records will be retained for at least three years after completion of the research.

VI. References

DoDD 3216.02
DoDD 2310.01E
32 CFR 219
Section 252 of Public Law 130-160

Section 1520a of Title 50
Sections 289g-289g-2 of Title 42, U.S.C.