Fred Hutch Cancer Center

Institutional Review Board

Policy/Procedure

Title:	Research Involving Department of Defense (DoD) Components
Version:	1.00
Effective Date:	February 3, 2025
Responsible Office:	Institutional Review Office (IRO)
Responsible Official / Approved By:	Meghan Scott, IRO Director

POLICY STATEMENT

It is the policy of the Fred Hutchinson Cancer Center (Fred Hutch) that for human subjects research involving Department of Defense (DoD) components, it will comply with the requirements of the DoD in addition to the Department of Health and Human Services (DHHS) requirements for the protection of human subjects regulations at 45 CFR 46 and committed to in the Federal Wide Assurance for the Protection of Human Subjects.

DEFINITIONS

See *HRP-001 - Glossary of Terms and Acronyms* for full definitions of the following:

Department of Defense Component

DoD-Affiliated Personnel

Exempt

Federalwide Assurance (FWA)

Human Subject

"Involving" DoD

Minimal Risk

Prisoner of War

Research Involving a Human Being as an Experimental Subject

PRINCIPLES/OVERVIEW

The purpose of this policy is to describe the additional Institutional Review Board (IRB) requirements necessary to comply with DoD requirements that pertain to the protection of human subjects in DoD-supported research. Fred Hutch does not review classified research. Fred Hutch does not review or allow human participant research involving the testing of chemical or biological agents, pursuant to Section 1520a of Title 50, United States Code (U.S.C.), without exception.

INDIVIDUALS AFFECTED BY THIS POLICY

The contents of this policy apply to Institutional Review Office (IRO) staff, IRB members, Fred Hutch investigators, and investigators from other institutions who submit research studies to the Fred Hutch IRB for review.

PROCEDURES

1. Federal Wide Assurance (FWA)

When Fred Hutch is engaged in non-exempt DoD-supported human subjects research, its Federal Wide Assurance (FWA) applies.[1] Fred Hutch has an approved FWA with the Office for Human Research Protections (OHRP). Refer to *HRP-115 - POLICY - Federalwide Assurance*. According to prior DoD requirements, Fred Hutch had a DoD Addendum to the FWA on file with the Department of the Navy. The DoD Addendum was maintained in IR File 5710B. A copy of the DoD Addendum to the FWA is available to research staff by contacting the IRO Assistant Director.

2. Department of Defense Supplement

All non-exempt human subjects research submitted for review by the Fred Hutch IRB which involves a DoD component must attached *HRP-263 - FORM - Department of Defense Supplement* to the study submission in Hutch IRB. The supplement applies to all non-exempt human subjects research (e.g., Full and Expedited IRB review). IRO staff will follow *HRP-360 - WORKSHEET - IRB Application (Contact), HRP-361 - WORKSHEET - IRB Application (No Contact)*, or *HRP-366 - WORKSHEET - Department of Defense (DoD) Supplement*, as appropriate.

3. Additional Requirements for Research Involving any Department of Defense Component

For research involving any DoD component the following additional requirements are necessary in addition to all other applicable IRB requirements under 45 CFR 46 and 21 CFR 50, 56, 312, and 812.

Note: If your DoD-funded research involves large-scale genomic data and will or may include participants who are DoD-affiliated personnel, please contact the IRO for guidance. Additional DoD component review may be required and protections applied.

a. Exempt or Not Human Research

For DoD-supported research that is exempt or does not involve human subjects, the principal investigator must submit all protocol documents along with institutional documentation of the determination that the research is either Not Human Research, exempt human subjects research, or limited IRB review to the Human Research Protection Office (HRPO) at the DoD component involved in the research.[2]

b. Non-Exempt Human Research

All research involving human subjects requires acceptance/approval by HRPO before the research may be initiated.

The principal investigator is responsible for submitting to the HRPO:

i. Documentation that the research has been reviewed and approved by an IRB, including scientific merit, amendments, and additional reviews;

ii. Documentation of key investigators' human research protection training;

iii. IRB-approval protocol documents;

iv. Current FWA and IRB registration numbers.[3]

c. Research requiring consent by a legal authorized representative (LAR)

For research involving a human being as an experimental subject, informed consent may be provided by legally authorized representatives (LARs) of subjects if: (1) the participant lacks capacity, due to age, condition, or other reason, to make a decision regarding consent to participate in the research; **AND** (2) the principal investigator intends, and the IRB has determined, that the research may hold the **prospect of direct benefit to the individual participants**.[4]

---

[1] DoD Instruction 3216.02, section 3.4.a(3), April 15, 2020
[2] DoD Instruction 3216.02, section 3.6.b(6)(b), April 15, 2020
[3] DoD Instruction 3216.02, section 3.6.b(6)(a), April 15, 2020
[4] DoD Instruction 3216.02, section 3.11.c, April 15, 2020

Examples of situations where LARs might provide consent: parents consenting on behalf of children; proxies or family members consenting on behalf of incapacitated participants.

d. Independent Research Monitor for greater-than-minimal risk research

Per DoD Instruction 3216.02 (November 8, 2011), an appointment of an independent research monitor was required for research involving more than minimal risk. The current DoD Instruction 3216.02 (April 15, 2020) no longer requires an independent research monitor for greater-than-minimal risk research. Studies approved with an appointed research monitor must continue to comply with the IRB-approved monitoring plan unless a modification is submitted to change it.

e. Additional protections for greater-than-minimal risk research involving participants who are DoD-affiliated personnel:

Per DoD Instruction 3216.02 section 3.9.f, for human subjects research involving DoD-affiliated personnel, the principal investigator must receive command or DoD Component approval to execute the research. Military and civilian supervisors, officers, and others in the chain on command shall not influence the decisions of their subordinates to participate or not to participate as research participants. Military and civilian supervisors, officers, and others in the chain of command shall 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.

When recruitment occurs in a group setting, an ombudsperson not connected in any way with the proposed research or the unit shall be present to monitor that the voluntary nature of individual participants is adequately stressed and that the information provided about the research is adequate and accurate. The ombudsperson should be available to address DoD-affiliated personnel's concerns about participating in the research.

For DoD civilians as subjects, DoD civilians must also follow their organization's policies regarding the requirement to obtain permission to participate in research.

f. Additional consent requirements:

The DoD requires additional elements of consent be provided to potential subjects unless the requirement to do so is waived by the DoD:

- A statement that the DoD or DoD component is funding the research; and
- A statement that representatives of the DoD are authorized to review research records.

If the human subjects research involves DoD-affiliated personnel as subjects 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. The informed consent document must also include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.[5]

g. Waivers of consent

Per 10 U.S.C. 980(b) and DoD Instruction 3216.02 section 3.11, the requirement to obtain prospective consent may not be waived for Research Involving a Human Being as an Experimental Subject unless such waiver is approved by the Assistant Secretary of Defense for Research and Engineering or the head of the DoD component involved in the research if appropriately delegated by the Assistant Secretary consistent with 3216.02 section 3.11. The Assistant Secretary of Defense for Research and Engineering, or delegate, may waive the requirements of informed consent for Research Involving a Human Being as an Experimental Subject 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 might directly benefit the individual experimental participant, and
- The research is conducted in compliance with all other applicable laws and regulations

[5] DoD Instruction 3216.02, section 3.9.f(1) and f(6)a, April 15, 2020

The IRB must be provided with documentation of the Assistant Secretary's, or delegate's, approval of the waiver.

For research not meeting the definition of Research Involving a Human Being as an Experimental Subject, the IRB may waive consent as described in 45 CFR 46.116(f).

h. Limitations on compensation to military personnel using DoD funds

DoD Instruction 3216.02 section 3.9.f(7) and the Dual Compensation Act limits compensation for U.S. military personnel participating in research during active-duty hours. This prohibition applies to U.S. military personnel paid from either appropriated or non-appropriated funds, or a combination thereof, and includes temporary, part-time and intermittent appointments. U.S. military personnel may not receive compensation for research while on active-duty hours. U.S. military personnel may be compensated for research if the participant is involved in the research while not on duty. If the research involves compensation for blood donations, payment cannot exceed $50 per blood draw (24 USC 30). Non-federal personnel may be compensated for research procedures other than blood draws in a reasonable amount approved by the IRB according to local prevailing rates and the nature of the research.

i. Surveys and interviews administered to DoD personnel

Research involving the administration of surveys to, or interviews of, DoD personnel (military or civilian) must be submitted, reviewed, and approved by the DoD component after the research is reviewed and approved by the IRB.

j. Research involving captured or detained prisoners of war

Per DoD Instruction 3216.02 section 3.9.e, research involving captured or detained prisoners of war is prohibited. Involvement of other detainees (e.g., civilian internees, retained persons, lawful and unlawful enemy combatants) as human subjects are also prohibited under DoD regulations. No research involving DoD which includes captured or detained prisoners of war or other detainees will be initiated at Fred Hutch.

k. Special Populations (Pregnant Women, Neonates, Prisoners, and Children)

Research involving pregnant women, neonates, prisoners, and children are subject to special protections under 45 CFR 46 Subpart B, C, and D. The Fred Hutch IRB applies these protections to all research projects (see *HRP-125 - POLICY - Research Involving Special Populations*). When reviewing research per DoD Instruction 3216.02, the following additional special considerations apply per DoD Instruction 3216.02 section 3.9:

- When a participant becomes pregnant, or when the principal investigator learns that a previously enrolled human subject is pregnant, and the research was not reviewed and approved by the IRB in accordance with 45 CFR 45, Subpart B, the principal investigator must promptly notify the IRB and the DoD HRPO.
- For purposes of applying Subpart B the phrase "biomedical knowledge" shall be replaced with "generalizable knowledge."
- The applicability of Subpart B is limited to the following:
    - Research involving pregnant women as participants that is more than minimal risk and includes interventions or invasive procedures to the women or the fetus; or
    - Research involving fetuses or neonates.
- Research involving fetal tissue must comply with USC Title 42, Chapter 6A, Subchapter III, Part H, 289g.
- In addition to the allowable categories of research on prisoners in Subpart C, epidemiological research is also permissible under DoD Instruction 3216.02 section 3.9.c. when:
    - The research describes the prevalence of incidence of a disease by identifying all cases, or studies potential risk factor associations for a disease,
    - The research presents no more than minimal risk,
    - The research presents no more than an inconvenience to the participant; and,

- Prisoners are not the particular focus of the research.

- When a participant becomes a prisoner in research involving a DoD component, and the research was not reviewed and approved by the IRB in accordance with 45 CFR 45, Subpart C, the principal investigator must promptly notify the IRB and the DoD HRPO and other federal agencies.
- Prisoner research, including for prisoners who become incarcerated during a research study, cannot be reviewed through the expedited procedure. There are no special requirements for DOD research involving children. Subpart D of the Common Rule is followed.
- The IRB is aware through this policy of the definition of “prisoner of war

4. Additional Requirements for Research Involving Department of Navy Component

For research involving Department of Navy the following additional requirements are necessary in addition to all other applicable IRB requirements under 45 CFR 46 and 21 CFR 50, 56, 312, and 812.

a. Surveys and interviews administered to Department of Navy personnel
A Privacy Act Statement must be displayed prominently on all Navy personnel surveys without exception regardless of whether personal identifiers are requested. The statement will identify the authority for survey administration (including OPNAV RCS), advise respondents of the purpose and routine uses of the survey, indicate that the survey is voluntary, explain the intended use(s) of the data, and describe measures used to safeguard confidentiality.

b. Independent scientific review prior to IRB review
Per SECNAVINST 3900.39D section 8(c)(6), research involving a Department of the Navy component requires an independent review of research for scientific merit or scholarship prior to IRB review. For clinical research, review by the Scientific Review Committee (SRC) satisfies this requirement. For other greater-than-minimal risk research, an equivalent review by an independent scientific review committee is required (e.g., NIH Peer review), and documentation provided to the IRB prior to review of the research. For non-clinical, minimal risk, and exempt research; review and approval by the division head is satisfactory to meet this requirement.

c. Compensation for Injury in greater than minimal risk research
Per SECNAVINST 3900.39D section 6(5), research involving a Department of the Navy component that is greater than minimal risk shall include an arrangement for emergency treatment and necessary follow-up of any research-related injury. The IRB will determine whether minimal risk research also might include a similar arrangement for research related injury as appropriate.

d. International research locations
Per SECNAVINST 3900.39D section 6(i), research involving human subjects who are not U.S. citizens or DoD personnel, conducted outside the United States, and its territories and possessions, requires permission of the host country. The laws, customs, and practices of the host country and those required by this instruction will be followed. An ethics review by the host country, or local Naval IRB with host country representation, is required. Fred Hutch investigators conducting international research involving DoD are required to submit documentation of local host country approval to conduct the research and documentation of local ethics review and approval.

e. Principal Investigators and IND/IDE research
Per SECNAVINST 3900.39D section 6(h), research involving DoD may not be sponsored by an investigator who also is the holder of the IND or IDE for which the research is being done.

5. Additional Requirements for Research Involving Department of Defense – Personnel and Readiness

For research involving Department of Defense – Personnel and Readiness the following additional requirements are necessary in addition to all other applicable IRB requirements under 45 CFR 46 and 21 CFR 50, 56, 312, and 812.

a. Human subjects training for research personnel

Per HA Policy 05-003, for research involving a DoD component which falls under the purview of the Under Secretary of Defense (Personnel and Readiness) all investigators and research staff directly involved in human subjects research shall have *Initial* and *Annual* training on human subjects protections, be familiar with this policy, the DoDI 3216.02 and any relevant materials specific to the DoD component.

6. Additional Institutional Reporting Requirements

a. Institutional Reporting Requirements for all DoD Components

Consistent with the institutional reporting requirements under DoD Instruction 3216.02 section 3.6.b(6)(d), all events requiring notification to outside institutions under *HRP-117 - POLICY - Requirements for Reporting to Institutional and External Officials* shall be copied to the HRPO at the DoD component involved in the research.

The following shall be reported by the IRO Director, or designee, to the DoD human research protection officer at the appropriate DoD component within 30 calendar days:

1. The organization is notified by any Federal body, State agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that any part of the Human Research Protection Program is under investigation for cause involving a DoD-supported research protocol.
2. Unanticipated problems involving risks to participants or others, suspensions, terminations, and serious or continuing noncompliance.

The Principal Investigator is responsible for submitting, at minimum, the following events to HRPO within 30 days:

1. IRB-approved changes to the human subjects research that involve changes to key investigators or institutions; decreased benefit or increased risk to subjects in greater than minimal risk research as defined in 32 CFR 219; addition of vulnerable populations, or DoD-affiliated personnel as subjects.
2. Results of IRB review of Continuing Review Reports.
3. Change in the reviewing IRB from Fred Hutch to an IRB at another assured institution.
4. The study's closure.

b. Additional Institutional Reporting Requirements for Department of Navy

The following specific events will be reported to Department of Navy (DoN) Human Research Protection Office for research involving Department of Navy consistent with SECNAVINST 3900.39D section 8(d)(2a-g).

1. All suspensions or terminations of previously approved DoN-supported research protocols.
2. The initiation and results of investigations of alleged non-compliance with human subject protections.
3. Unanticipated problems involving risks to subjects or others, or serious adverse events in DoN-supported research.
4. All audits, investigations, or inspections of DoN-supported research protocols.
5. All audits, investigations, or inspections of the institution's HRPP conducted by outside entities (e.g., the FDA or OHRP).
6. Significant communication between institutions conducting research and other federal departments and agencies regarding compliance and oversight.
7. All restrictions, suspensions, or terminations of institutions' assurances.

7. Records Inspection, Copying and Recordkeeping:

Per DoD Instruction 3216.02, section 3.6.b(6)(d)9, records relating to research involving a DoD component will be made accessible for inspection and copying by representatives of the DoD. This will include documentation relating to the institution's compliance or non-compliance with DoD requirements.

DOD may require submitting records to DOD for archiving. Investigators should consult with the HRPO regarding record-keeping requirements for their research.

SUPPORTING DOCUMENTS

HRP-001 - Glossary of Terms and Acronyms

HRP-115 - POLICY - Federalwide Assurance

HRP-117 - POLICY - Requirements for Reporting to Institutional and External Officials

HRP-125 - POLICY - Research Involving Special Populations

HRP-263 - FORM - Department of Defense Supplement

HRP-360 - WORKSHEET - IRB Application (Contact)

HRP-361 - WORKSHEET - IRB Application (No Contact)

HRP-366 - WORKSHEET - Department of Defense (DoD) Supplement

REFERENCES

32 CFR 219, Department of Defense Regulations, “Protection of Human Subjects” (DoD adoption of the “Common Rule”)

45 CFR 46 Department of Health and Human Services Regulations, “Protection of Human Subjects,” Subparts B, C, and D as made applicable by DODD 3216.02

21 CFR 50, 56, 312, and 812

DoD Instruction (DoDI) 3216.02, “Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and -Supported Research” April 15, 2020

Title 10 United States Code Section 980 (10 USC 980), “Limitation on Use of Humans as Experimental Subjects”

Title 24 United States Code Section 30 (24 USC 30), “Payment to Donors of Blood for Persons Undergoing Treatment at Government Expense”

DoDD 3210.7, “Research Integrity and Misconduct”

DoDD 6200.2, “Use of Investigational New Drugs in Force Health Protection”

Department of the Navy:

SECNAVINST 3900.39D of 6 November 2006

Department of the Army;

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

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

AR 40-7, Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances, 4 January 1991

Department of the Air Force:

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

Office of the Secretary of Defense for Personnel and Readiness:

HA Policy 05-003

VERSION HISTORY

Version	Effective Date
-	-