Purpose and Background

This page provides guidance for researchers and IRBs about special requirements for conducting and reviewing human subjects research involving any component of the Department of Defense (DoD).

In 2006, the DoD enhanced its human subject protection requirements. UCSF has signed an Addendum [1] to its Federalwide Assurance (FWA) that it will apply Department of Defense (DoD) regulations and policies for the protection of human research subjects when conducting, reviewing, approving, overseeing, supporting or managing human subjects research involving the DoD. A copy of the DoD/DoN Addendum to UCSF? s Federalwide Assurance
Responsibility for upholding DoD requirements for human subjects research is shared between researchers and their teams, the University administration and the DoD.

You will be asked to complete the "Department of Defense (DoD) Supplement" in IRB Application in iRIS if your research involves the DoD.

What Qualifies as DoD Research

Research is considered to involve the DoD when:

- **Funding**: The research is funded by a component of DoD. Example: A grant from the Office of Naval Research.
- **Collaboration**: The research involves cooperation, collaboration or other type of agreement with a component of DoD. Example: An Army Medical Laboratory will conduct malaria antigen detection tests for study.
- **Facilities**: The research uses property, facilities or assets of a component of DoD.
- **Personnel**: The subject population will intentionally include personnel (military and/or civilian) from a component of DoD. Note: DoD policies and requirements do not apply when DoD personnel incidentally participate as subjects in research that is not supported by DoD, and DoD personnel are not an intended population of the research.

List of DoD components

The DoD components include, but may not be limited to:

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

For research sponsored by the DoD, ?experimental subject? is defined as 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 (32CFR.210.102). Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject’s environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

**Instructions for all DoD Research**

DoD-related research typically requires additional compliance activities, documentation and subject protections. You should anticipate and plan for these requirements, which may require significant coordination of timing and activities among offices and institutions.

This information and guidance applies to all human subjects research involving the DoD, with the following exception: for human subjects research that qualifies for exemption [3], the only part of this guidance that applies is the requirements for DoD Funding Release described below.

**DoD Funding Release**

Researchers are not allowed to expend DoD funds for human subjects research until all of the following requirements have been met:

- The IRB has reviewed and approved the research (or granted an exemption).
- Research Management Services (RMS) has provided any materials requested by the DOD funding agency.
- RMS has been authorized by DoD to activate the award.

**Researchers have the following responsibilities for non-exempt research involving the DoD:**

**Education**

The DoD education and training requirements exceed the requirements of UCSF.

**Initial education and training:**

- As described by DoD, ?all personnel involved in reviewing, approving, supporting, conducting, managing, or overseeing research involving human subjects must complete initial and ongoing research ethics and human subjects protections training appropriate to each individual’s level of involvement, duties, and responsibilities.? [Secretary of Navy SecNav Instruction 3900.39D]
- This requirement can be fulfilled through certification of UCSF CITI [4] training or the NAVY CITI [5] training.

**Continuing education and training:**

- DoD requires continuing education every three years. Researchers and appropriate research staff should plan to recertify UCSF or Navy CITI Training appropriately.

Scientific merit review
The Army and the Navy require independent scientific review and approval **prior to IRB review** of new applications and substantive modifications. This requirement does not apply to research involving other components of the DoD.

**Who conducts the review?** A scientific review conducted by a funding agency (including DoD) or by an established internal review mechanism in the researcher?s school or department will satisfy this requirement. In the absence of such a review, an *ad hoc* scientific review may be provided by the researcher?s chair or dean.

**What topics should the review cover?** DoD refers researchers to the National Naval Medical Center scientific review template and to the Army?s description of scientific review criteria in its Human Research Protections Office Policies and Procedures. These are essentially the same as the scientific review conducted by any federal funding agency. An internal or ad hoc review should cover the same topics, including:

- **Significance:** Does the research address a problem of scientific and/or practical importance? If the aims of the research are achieved, how will scientific knowledge be advanced? What effect will the research have upon the concepts or methods that drive this field of research? Will there potentially be important practical benefits to military and/or civilian communities? Is the research question articulated with clarity and precision? Does the background section describe why the research question is important? Is the literature review comprehensive and complete?
- **Approach:** Are the conceptual framework, design, methods and analyses adequately developed, feasible, well-integrated and appropriate to the aims of the study? Are the controls adequate? Does the researcher acknowledge potential problem areas and consider alternative tactics? Is the proposed sample size and statistical analysis valid?
- **Researcher:** Is the researcher appropriately trained to conduct the research? Is the work proposed appropriate to the experience level of researcher associates?
- **Environment:** Does the scientific environment in which the study will be done contribute to the probability of success? Does the proposed study take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Are the facilities available and appropriate?

**Documentation of the review.** The IRB must be provided with written documentation of the scientific review that summarizes the scientific issues raised and addressed during the review, together with a statement that names and describes the reviewers. Examples of appropriate documentation include: copy of a review summary from a federal agency; or a memo from the researcher?s department chair.

**Medical monitor**

A research monitor is required for research involving greater-than-minimal risk to subjects.

**Definition of minimal risk:** 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 IRB is responsible for making this determination.
The monitor: A medical monitor or a non-medical monitor? The written guidance from DoD focuses on medical risks. However, DoD has advised another institution that if a medical monitor would not be appropriate for the research, then a non-medical monitor may be appointed.

DoD guidance about the monitor, from Department of Defense Directive 3216.2:

- For research involving more than minimal risk (as defined in 32 CFR 219.102(i)), an independent medical monitor shall be appointed by name. Medical monitors shall be physicians, dentists, psychologists, nurses, or other healthcare providers capable of overseeing the progress of research protocols, especially issues of individual subject/patient management and safety. Medical monitors shall be independent of the investigative team and shall possess sufficient educational and professional experience to serve as the subject/patient advocate.
- Depending on the nature of the study, the medical monitor may be assigned to assess one or more of the following phases of a research project: subject recruitment; subject enrollment; data collection; or data storage and analysis.
- At the discretion of the IRB, the medical monitor may be assigned to discuss research progress with the principal investigator, interview subjects, consult on individual cases, or evaluate adverse event reports. Medical monitors shall promptly report discrepancies or problems to the IRB. They shall have the authority to stop a research study in progress, remove individual subjects from a study, and take whatever steps are necessary to protect the safety and wellbeing of research subjects until the IRB can assess the medical monitor?s reports.

Documentation

Researcher files: Researchers are required by DoD policy to maintain an extensive number of research-related and compliance-related documents in their files. Researchers are responsible for fulfilling these requirements, which typically begin by contacting DoD to learn about the requirements.

DoD documentation requirements: It is the responsibility of the researcher to provide DoD with all documents required by DoD. For example, the sponsoring DoD agency may require the submission of records to the DoD for archiving.

Documentation of exemption: The researcher should document the determination by the IRB whether research meets the research criteria for exemption.

International research requirements

DoD-related research that involves subjects who are not U.S. citizens or Department of Defense personnel must obtain and provide:

- Permission of the host country.
- Ethics review and approval by the host country or by a local Naval IRB with host country representation.
• Additional safeguards might not be applicable to social-behavioral research involving no more than minimal risk.

Responsibilities when collaborating with other institutions

**Informing the IRB:** Researchers are responsible for informing the UCSF IRB of any collaborative arrangements with other institutions or individuals not at UCSF. This information is important for ensuring that the researcher and UCSF fully comply with DoD requirements.

**Advance consultation with IRB is encouraged:** Because such arrangements may need DoD review, researchers are strongly encouraged to consult with the UCSF IRB when submitting an application.

**Required documentation:** Researchers are responsible for providing the IRB with appropriate documentation about the involvement of other institutions in cases of collaborations or multi-site research. When UCSF is the lead organization for DoD-related research, these documents must include a specific statement of compliance with the DoD human subject protection requirements and the DoD Addendum to UCSF’s Federalwide Assurance.

**Research-related injuries involving collaborating institutions:** Collaborating institutions must have arrangements for emergency treatment and necessary follow-up of any research-related injury of subjects in research involving greater-than-minimal risk, to protect human subjects from medical expenses that are the direct result of participation in research. If UCSF is the lead organization, then the IRB must evaluate adherence to this requirement across all performance sites.

**Additional protections for military research subjects**

DoD requires the following protections for military personnel being recruited for research that involves greater-than-minimal risk.

• Officers are not permitted to influence the decision of their subordinates.
• Officers and senior non-commissioned officers may not be present at the time of recruitment.
• Officers and senior non-commissioned officers have a separate opportunity to participate.
• During recruitment briefings to a unit where part of the unit is being recruited, an independent ombudsman is present.
• Limitations on dual compensation prohibit an individual from receiving pay from more than one position for more than 40 hours of work in one calendar week, which includes temporary, part-time, and intermittent appointments.

Informed consent by a legally authorized representative

Per military law and DoD directive, informed consent may be provided by a legally-authorized
representatives of subjects if: (1) the subject lacks capacity, due to age, condition, or other reason, to make a decision regarding consent to participate in the research; AND (2) the IRB has determined that the research is intended to be beneficial to the individual subjects.

Waiver of consent

The requirement to obtain consent cannot be waived for any research involving the DoD, and 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, except under one of the following conditions:

- The research is intended to be beneficial to the subject, the subject lacks the capacity to provide consent, and a legally-authorized representative will provide consent. *Examples*: young minors, cognitively impaired individuals.
- The Head of the DoD component involved in the research may waive the requirement for consent with respect to a specific project, in order to advance the development of a medical product necessary to the Armed Forces, but only if the research may directly benefit the subject and the research is carried out in accord with all other applicable laws and regulations (such as 21 CFR 50.24).
- This prohibition does NOT apply to screening (sometimes called “pre” screening) of records to identify possible subjects. The IRB can grant a waiver of consent for such activities.

Compensation

Researchers must comply with limitations on dual compensation for U.S. military personnel.

Survey research

Research involving the administration of surveys to, or interviews of, DoD personnel (military or civilian) may require DoD approval of the surveys or interview questions.

Compliance and misconduct

The Naval command or activity with responsibility for the research will review all allegations of non-compliance with human subject protections and take action if appropriate. The HRPP will report the initiation of all investigations and report results regardless of the findings to the Navy SG and appropriate sponsors. [SecNavInst 3900.39D]

Address and report allegations of research misconduct

The Naval command or activity with responsibility for the research will review all allegations of research misconduct and take action if appropriate. The HRPP will report the initiation of all investigations and report results regardless of the findings to the Navy SG and appropriate sponsors. [SecNavInst 3900.39D]

Research involving prisoners
The IRB is prohibited from approving research involving prisoners of war. IRBs must be aware of the definition of ?prisoner of war? for the Department of Defense component granting the addendum.

**Post-Approval Instructions**

Review these instructions before submitting the types of submissions listed below.

**Reporting subject injury and adverse events**

Report unanticipated problems, adverse events, research-related injury and suspensions or terminations of research.

**Continuing review**

Annual continuing review is required for studies involving the DoD. The following items should be submitted to the IRB in addition to the standard Continuing Review requirements.

- **Continuing education**: As described above, DoD requires continuing education related to human subjects for the researchers and appropriate research staff. This requirement may be fulfilled by recertifying UCSF or Navy CITI training.
- **Research results**: DoD requires that the researcher provide the IRB with copies of publications, presentations and reports resulting from the research. These should be provided to the IRB with scheduled continuing review information.

**Modifications**

If an amendment involves substantive changes (e.g., new procedures, a new subject population, a new aim), the researcher should upload the documentation of scientific review and approval of the changes in the amendment.

- If the research was not previously DoD-related but the amendment will make the project DoD-related, the researcher must note this in the Modification Form.
- The researcher is responsible for notifying DoD and the IRB of any audits, investigations or inspections of DoD-related research.

**IRB and OVPR Responsibilities**

**Advice and guidance**

Upon request, IRB staff and OEVC are responsible for providing researchers and research staff with advice and guidance about the IRB review of DoD-related research.

**Identification of DoD-related research**
IRB staff and IRB members screen and/or review IRB application materials to identify DoD-related research.

Collaborative agreements

OVPR will establish and document collaborative agreements with other institutions or non-UCSF individuals engaged in DoD-related research.

Additional information

IRB staff contact the researcher or research staff if necessary, to obtain missing information or documents, clarification, or (if necessary) a revised application.

DoD-regulated research involving prisoners

- The IRB is prohibited from approving research involving prisoners of war.
- IRBs must be aware of the definition of ?prisoner of war? for the Department of Defense component granting the addendum.

Initial review

Mandatory IRB determinations. In addition to checking the application for full compliance with DoD regulations, the IRB is required to make the following formal determinations for all DoD-related research. The determinations are documented in iRIS and in the IRB minutes:

**Air-Force research focus areas:** One or more of the following five possibilities are identified in the application as the research focus area:

- Medical Readiness
- Prevention (primary, secondary, tertiary)
- Medical Utilization
- Managed Care
- Treatment, Diagnosis, or Other

**Level of research risks:** Does the research involve more than minimal risk to subjects, as defined in DoD human subjects regulations? The criteria for level of IRB review (i.e. Expedited vs. Full Committee) are the same for DoD related research as for non-DoD related research.

**Research monitor:** For research involving more-than-minimal risk, is the research monitor appropriate with regard to: type of monitor; qualifications; and roles and responsibilities?

- **Benefits:** Is the research designed to be beneficial to the individual subjects when the subject lacks the capacity to make a decision regarding consent to participate and a legally-authorized representative provides the research consent?
• **Disclosure**: Does the disclosure include provisions for research-related injury that follow the requirements of the DoD component?

Amendment/modification review

*Research that is already DoD-related (i.e., prior to the modification request) and that has already been reviewed by the UCSF IRB as DoD-related.*

- The IRB staff screen the Modification Form, within the context of the existing DoD Supplement in the IRB Application.

  a) If the Supplement no longer accurately reflects the research, IRB staff ask the researcher to revise the Supplement (and any additional documentation).

  b) If the modification involves substantive changes, IRB staff ensures that the researcher provides documentation of scientific review and approval of the modifications.

*Research that has not been DoD-related, but that becomes DoD-related because of the requested modification.*

- If the initial application was reviewed by the full IRB, then the modification must also be reviewed by the full IRB because a new set of regulations is involved.
- IRB staff ensures that the researcher has provided the information to address all procedures and populations that are DoD-related.

Continuing review

**Screening**: IRB staff screen the scheduled continuing review application to ensure that the following two DoD requirements have been fulfilled. If not, the staff contacts the researcher so that the requirements can be met before the IRB review.

- **Continuing Education**: The DoD continuing education requirement has been met.
- **Research Results**: DoD requires that the researcher provide the IRB with copies of publications, presentations, and reports resulting from the research. Per UCSF policy for all research (whether or not DoD-related), these should be provided to the IRB at the time of continuing review.

Records and reporting obligations

OVPR is required to report to DoD any of the following events or situations that occur for DoD-related research:

- Serious or continuing non-compliance
- Suspension or termination of research
- Unanticipated problems involving risks to subjects or others
- Significant communication between institutions conducting research and other federal
departments and agencies, regarding compliance and oversight

*The DoD FWA number must be provided in the letter.

**When a specific situation involves reporting to more than one federal agency, the letter is addressed to the primary federal agency (typically OHRP or FDA), and a copy is sent to DoD.

**Additional Information and Regulatory Citations**

| Department of the Navy Human Research Protection Program [5] (DoN HRPP) | Secretary of the Navy Instruction 3900.39D [8] |
| Regulatory citations |

32 CFR 219, Protection of Human Subjects?

Department of Defense (DoD) Directive 3216.2, Protection of Human Subjects and Adherence to Ethical Standards in DoD Supported Research?

Department of Defense Directive 5500.7-R, Joint Ethics Regulation, Standards of Conduct?

Department of Defense (DoD) Instruction 6200.02, Application of Food and Drug Administration (FDA) Rules to Department of Defense Force Health Protection Programs, February 27, 2008.


Secretary of the Navy, SECNAV INSTRUCTION 3900.39D, Human Research Protection Program?. National Naval Medical Center Scientific Review Template, revision 12-15-06.


Army Regulation 70-25, January 25, 1990; Use of Volunteers as Subjects of Research? Air Force Instruction 40-402, Protection of Human Subjects in Biomedical and Behavioral