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Chapter 3 Federal Regulations and State Laws

This chapter provides an overview of the federal regulations and California law that govern human subjects research at USC. These include: Health and Human Services, Defense, Justice, Energy, Education and California law. The chapter concludes with a brief discussion of California laws that impact human subjects research.

3.1 Department of Health and Human Services (DHHS)

Common Rule ([45 CFR 46](#))

In 1981, in response to the Commission’s reports and recommendations, both the Department of Health and Human Services (DHHS, formerly DHEW) and the FDA promulgated significant revisions of their human subjects regulations. The revisions were concerned with details of what the IRB is expected to accomplish and some of the procedures it must follow.

The DHHS regulations are codified at [Title 45 Part 46](#) of the Code of Federal Regulations. Those “basic” regulations became final on January 16, 1981, and were revised effective March 4, 1983, and June 18, 1991. The June 18, 1991, revision became the adoption of the Federal Policy for the Protection of Human Subjects. The Federal Policy (or “Common Rule,” as it is sometimes called) was jointly promulgated by the sixteen federal agencies that conduct, support, or otherwise regulate human subjects research; the FDA also adopted many of its provisions. As is implied by its title, the Federal Policy is designed to make uniform the human subjects protection system in all relevant federal agencies and departments that adopt it. The “common” part of title 45 part 46 is also known as subpart A.

*Additional federal agencies/departments have since adopted [45 CFR 46](#).

- [Subpart A](#), “Basic HHS Policy for Protection of Human Research Subjects”, revised effective June 23, 2005.

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Additional protections for various vulnerable populations have been adopted by DHHS in the subparts of title 45 Part 46 as:

- [Subpart B](#), “Additional Protections Pertaining to Research, Development, and Related Activities Involving Fetuses, Pregnant Women and Human In vitro Fertilization” revised effective November, 2001.
- [Subpart C](#), “Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects” became final on November 16, 1978.
- [Subpart D](#), “Additional Protections for Children Involved as Subjects in Research” became final on March 8, 1983, and was revised for a technical amendment on June 18, 1991.

FDA (21 PARTS 50 AND 56)

Food and Drug Administration (FDA) regulations on the protection of human subjects are codified at [Title 21 Parts 50](#) and [56](#) of the Code of Federal Regulations. **Part 50**, which sets forth the requirements for informed consent. Subpart C provides special protections for prisoners. Subpart D provides Additional Safeguards for Children in Clinical Investigations. **Part 56** sets forth the provisions for Institutional Review Boards.

Additional FDA regulations that are relevant to IRB review of research are **Parts 312** (Investigational New Drug Application), [600](#) (Biological products), [812](#) (Investigational Device Exemptions) and [860](#) (Medical Device Classification Procedures).

For a comparison of FDA and HHS Human Subject Protection Regulations, click [here](#).

For additional information about FDA-regulated research, refer to [Chapter 18 – FDA-Regulated Research](#).

HIPAA (45 PARTS 160 AND 164)

The HIPAA Privacy Rule is under the jurisdiction of the Office of Civil Rights which is responsible for interpreting, establishing guidelines, and any subsequent modifications of the rule. Information regarding the most recent version of the Privacy Rule - Health Information Technology for Economic and Clinical Health (HITECH Act), may be found at: <http://www.hhs.gov/about/news/2013/01/17/new-rule-protects-patient-privacy-secures-health-information.html>

3.2 Department of Defense (DOD) and Department of the Navy (DON)

The Department of the Navy (DoN) supports research involving human subjects conducted by a non-DoD institution by way of contracts, grants, assistance agreements, cooperative agreements, cooperative research and development agreements and other partnering agreements. As of February 1st, 2016, DoN no longer required or issued the Navy Addendum to the FWA. DoN implements human research protection requirements through the Common Rule (32 CFR 219), Department of Defense Instructions ([DoDI 3216.02](#)) and directives, and DoN instructions ([SECNAVINST 3900.39D](#)). The DoD and DoN also have additional requirements for research involving human subjects, including the requirement for review by a Human Research Protection Official (HRPO).

Researchers should be cognizant that DOD requirements may lead to additional costs related to the conduct of the study.

Researchers are urged to anticipate any specific subject protection costs that might be directly associated with the DOD project. For example, if a project poses greater-than-minimal risk and therefore requires a Research Monitor, costs associated with the monitor might qualify as direct costs. For assistance in identifying such costs and dealing with the funding agency, please consult with the USC Office of Contracts & Grants for assistance.

Note: If you are designing a project that will involve other entities as collaborators or sub-contractors, you are strongly encouraged to consult with the DOD or the sponsor to identify additional requirements.

Research Supported by the Department of Defense (DOD)

When submitting a study to the USC IRB that is supported by or in collaboration with DOD, specific additional information must be included in the iStar application. In addition to IRB requirements, federal regulations, state laws and institutional policies, the DOD (including the Navy, Army, Air Force, and Personnel and Readiness) requires the Institution to:

- Conduct initial and continuing research ethics education for personnel who are engaged in human subject research (who review, approve, oversee, or manage research)

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- Document determination by a designated staff person (other than investigators) whether research meets criteria for exemption
- Ensure new research and substantive scientific amendments to approved research shall undergo scientific review and that the review is considered by the IRB
- Ensure additional protections for military research subjects to minimize undue influence
- Explain to subjects any provisions for medical care for research-related injury
- Report unanticipated problems, adverse events, research-related injury, and suspensions or terminations of research within 30 days from the determination that the event is reportable
- Appoint a Research Monitor when necessary
- Safeguard for research conducted with international populations
- Protect pregnant women, prisoners, and children
- Comply with DOD limitations and modifications to research with pregnant women, fetuses and neonates [refer to [“Research Supported by the Department of Defense \(DOD\)”](#) in [Section 14.2 – Pregnant Women, Fetuses and Neonates in Research \(45 CFR 46 Subpart B\)](#)]
- Include women and minorities as subjects, if study is a clinical investigation including Armed Services personnel
- Comply with DOD limitations on research where consent by legally authorized representatives is proposed
- Comply with DOD limitation on exceptions from informed consent (10 USC 980, 45 CFR 46, and 21 CFR 50)

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- Comply with limitations on dual compensation for U. S. military personnel
- Follow DOD requirements for additional review for DOD-sponsored survey research or survey research within DOD
- Address and report allegations of non-compliance with human research protections
- Address and report allegations of research misconduct
- Follow procedures for addressing financial and other conflicts of interest
- Prohibit research with prisoners of war (POW) and detainees
- Comply with all provisions for research with human subjects using investigational test articles (drugs, device, and biologics)
- Follow recordkeeping requirements
- Support oversight by the sponsoring DOD Component (which may include DOD Component review of the research and site visits)

An explanation of some of the additional requirements follows:

Researcher Responsibilities

To ensure the DOD component conducts an administrative review, PIs are responsible for submitting documentation to the DOD Human Research Protection Official (HRPO) prior to starting a USC IRB-approved study.

Additionally, the following shall be reported promptly (within 30 days) to the DoD Human Research Protection Official:

- Significant changes to the research protocol approved by the IRB
- Results of the IRB continuing review
- Change of reviewing IRB

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- Notification by any Federal department, agency or national organization that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol
- Any suspension or termination of DoD-supported research

Potential for Undue Influence

The military structure expects loyalty and participation and thus has the potential to unduly influence a prospective subject's decision about whether to participate in research. Commanding Officers (CO) should be alert to the potential for undue influence in research with those in employer-employee status (worker), teacher-student, supervisor-subordinate relationships, or deployed active duty personnel. Regardless of the risk level of the research, no superiors (civilian supervisors, officers, and noncommissioned officers (NCOs)) shall influence the decisions of their subordinates (junior enlisted personnel) whether to participate as research subjects.

“Minimal Risk” Interpretation

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 should 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).

Research Monitor

A research monitor is required for all research involving greater than minimal risk. The IRB may determine that a research monitor is appropriate for other research. A research monitor has the authority to stop a research study, remove individuals from a study, observe group recruitment, and take whatever steps are necessary to protect the safety and well-being of participants. The IRB must approve the research monitor by name and a written summary of the monitors' duties, authorities, and responsibilities. When a research monitor is required, consult with the IRB Chair.

Research Related Injury Compensation

Every research protocol involving greater than minimal risk shall provide an arrangement for emergency treatment and necessary follow-up of any research-related injuries to subjects. IRBs will determine whether research involving minimal risk also might include a similar arrangement for research-related injury. Subjects should be informed about how the costs for research related injuries will be covered.

Waiver of Informed Consent Prohibited

If the research involves an intervention or interaction with subjects a waiver of consent or parental permission is prohibited unless a waiver is obtained from the Secretary of Defense.

International Research

If the research involves human subjects who are not US citizens or DOD personnel, it is conducted outside the United States, and its territories and possessions additional DOD requirements must be met.

Military and Civilian Personnel in Research

Civilian personnel may experience "pay check" vulnerability when research is conducted in the workplace. In addition, research findings may have unintended consequences for military and civilian personnel, such as loss of job, career, or benefits. Those involved in the research enterprise must recognize that non-participation may have subtle consequences and make every effort to avoid even the appearance of undue influence or coercion.

“Minors” in the Military

Individuals may join the military with parental permission when they are less than the state-mandated age of majority (generally 18 years). However, military members who are considered minors under state law must have parental permission, in addition to their assent, to participate in research.

Research with Data, Documents, Records, and Specimens

Access to data, documents, records, and specimens for research purposes requires IRB review. Examples include: mishap reports, blood specimens, training records, medical records, performance evaluations, employee records, fitness results, diving records.

Women in the Military

Federal regulations encourage women of childbearing potential to participate in drug development trials, but require additional safeguards.

State Laws

Military commands must comply with relevant state laws.

Research with Investigational Agents (Drugs, Devices, and Biologics)

In addition to complying with DOD/DON regulations for research on investigational drugs, devices, and biologics, investigators must also adhere to the Food and Drug Administration regulations (21 CFR Part 56 - IRBs and 21 CFR Part 50 - Informed Consent). The FDA and DOD regulations on basic requirements for IRBs and for informed consent generally are consistent.

Research Supported by the Department of the Navy (DON)

Studies that are supported by (or done in collaboration with) the Department of the Navy (DON) are subject to requirements in addition to those imposed by the Department of Defense as described below.

Researcher Responsibilities

PIs are responsible for submitting documentation to DON prior to starting an IRB-approved study and upon subsequent reviews by the IRB (addenda, continuing reviews). DON uses such documentation to conduct a “headquarters-level administrative review.”

Investigators should always report any serious adverse events, noncompliance, unanticipated problems involving risks to subjects or others, and protocol deviations and actions taken regarding the reports to the DON.

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Two DON components have documentation requirements. See the following links for the documentation requirements of each (note that the requirements differ):

- [Office of Naval Research \(ONR\)](#)
- [Department of the Navy Human Research Protections Program \(DON HRPP\)](#)

IRB Reporting Requirements

The IRB may be required to notify DON and the sponsor (if there is a non-DON sponsor) of serious adverse events, noncompliance, unanticipated problems involving risks to subjects or others, and protocol deviations and actions taken regarding the reports.

The DON must be notified of any audits, investigations or inspections of DON-supported research. IRB will report such inspections to DON only when the IRB conduct or are aware of the inspection.

DON HRPP requires certain IRB documentation to be submitted that is not maintained by the PI (such as IRB meeting minutes). The IRB will provide the PI with a copy of this documentation, and it is the PI's responsibility to provide this information to the DON HRPP directly.

The contact information for submission to ONR is provided at the ONR website above. The contact information for submission to the DON HRPP is:

Department of the Navy
Office of Research Protection (M00R)
Bureau of Medicine and Surgery
2300 E St., NW
Washington, DC 20372-5300
Fax: 202-762-0976 E-Mail: humanresearch@us.med.navy.mil

For additional information, refer to [Appendix K – Requirements for Department of Defense \(DOD\) Supported Research](#).

DON Personnel as Subjects

DON policies do not apply when DON personnel are not the targeted subject population but incidentally participate as subjects in a project that is not supported by the DON.

Publications

DON requires that the IRB receive and maintain copies of publications, presentations or reports based on the research protocol. Please include such items (if any) when submitting an application for continuing review or closing the study in iStar.

Questions

If you have questions regarding Navy requirements, please contact the IRB for assistance.

Helpful Links:

- Department of Defense Directive 3216.02: “Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research”
<http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf>
- Department of Defense Directive 3210.7: “Research Integrity and Misconduct”
<http://www.dtic.mil/whs/directives/corres/pdf/321007p.pdf>
- Electronic Code of Federal Regulations 32 CFR 219 – Department of Defense
http://www.ecfr.gov/cgi-bin/text-idx?tpl=/ecfrbrowse/Title32/32cfr219_main_02.tpl
- Secretary of the Navy Instruction 3900.39D, Section 4(a)(1) – Human Research Protection Program
http://fas.org/irp/doddir/navy/secnavinst/3900_39d.pdf

3.3 Department of Justice (DOJ)

When research is supported by the Department of Justice, USC fulfills its obligations with regard to the assurances and certification required by 28 CFR 46. The specific requirements for research supported by the Bureau of Prisons and National Institute of Justice are listed below.

Research Supported by the Bureau of Prisons

Compliance with 28 CFR 512

USC, USC IRBs, and researchers and research staff must follow the requirements of 28 CFR 512, including:

- The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
- The research design must be compatible with both the operation of prison facilities and protection of human subjects. The researcher must observe the rules of the institution or office in which the research is conducted.
- Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512.
- All research proposals will be reviewed by the Bureau Research Review Board.

Pilot Projects are not Considered Research

Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.

Research Design

The project must have an adequate research design and contribute to the advancement of knowledge about corrections.

Subject Selection and Incentives

The selection of participants within any one organization must be equitable. Incentives may not be offered to help persuade inmate participants to participate. However, soft drinks and snacks to be consumed at the test setting may be offered. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research participants who are both no longer in Bureau of Prisons custody and are participating in authorized research being conducted by Bureau employees or contractors.

Confidentiality

A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.

Except as noted in the consent statement to the participant, the researcher must not provide research information that identifies a participant to any person without that participant's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.

Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.

If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.

Disclosure and Informed Consent

Required elements of disclosure include:

- Identification of the researchers
- Anticipated uses of the results of the research
- A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable)
- A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a researcher may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant is an inmate, indicates intent to leave the facility without authorization

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- A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility

Research Proposal Requirements

When submitting a research proposal, the applicant shall provide the following information:

- A summary statement, which includes:
 - Names and current affiliations of the researchers
 - Title of the study
 - Purpose of the study
 - Location of the study
 - Methods to be employed
 - Anticipated results
 - Duration of the study
 - Number of participants (staff or inmates) required and amount of time required from each
 - Indication of risk or discomfort involved as a result of participation
- A comprehensive statement, which includes:
 - Review of related literature
 - Detailed description of the research method
 - Significance of anticipated results and their contribution to the advancement of knowledge
 - Specific resources required from the Bureau of Prisons
 - Description of all possible risks, discomforts, and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomforts will actually occur
 - Description of steps taken to minimize any risks
- Description of physical or administrative procedures to be followed to:
 - Ensure the security of any individually identifiable data that are being collected for the study
 - Destroy research records or remove individual identifiers from those records when the research has been completed
- Description of any anticipated effects of the research study on organizational programs and operations
- Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules

- A statement regarding assurances and certification required by 28 CFR 46, if applicable.

Investigator Requirements and Responsibilities

- The researcher must have academic preparation or experience in the area of study of the proposed research.
- The researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher.
- At least once a year, the researcher shall provide the chief, Office of Research and Evaluation, with a report on the progress of the research.
- At least 12 working days before any report of findings is to be released, the researcher shall distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance. The researcher shall include an abstract in the report of findings.
- In any publication of results, the researcher shall acknowledge the Bureau's participation in the research project.
- The researcher shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
- Prior to submitting for publication, the results of a research project conducted under this subpart, the researcher shall provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.

Research Supported by the National Institute of Justice (NIJ)

Privacy Certificate

All projects are required to have a privacy certificate approved by the NIJ Human Subjects Protection Officer. Under a privacy certificate, researchers and research staff do not have to report child abuse unless the participant signs another consent form to allow child abuse reporting.

Confidentiality Statement

All researchers and research staff are required to sign employee confidentiality statements, which are maintained by the responsible researcher.

Disclosure and Informed Consent

The confidentiality statement on the consent form must state that confidentiality can only be broken if the participant reports immediate harm to participants or others.

National Archive of Criminal Justice Data

A copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.

3.4 Department of Energy (DOE)

When research is supported by the Department of Energy, USC fulfills its obligations with regard to the assurances and certification required by 28 CFR 0 443.1B. The specific requirements for research supported by the Department of Energy are listed below.

Human Subjects Research

- Research involving human participants also includes studies of the intentional modification of the human environment; generalizable includes the study of tracer chemicals, particles or other materials to characterize airflow.
- Generalizable also includes studies in occupied homes or offices that:
 - Manipulate the environment to achieve research aims
 - Test new materials
 - Involve collecting information on occupants' views of appliances, materials, or devices installed in their homes or their energy-saving behaviors through surveys and focus groups
 - Generalizable should be viewed in terms of the contribution to knowledge within the specific field of study

Personally Identifiable Information

Researchers are required to follow DOE requirements for the protection of personally identifiable information by completing and complying with the requirements of the [“Checklist for IRBs to Use in Verifying That HS Research Protocols Are in Compliance with DOE Requirements.”](#)

Reporting Requirements

Researchers must promptly (**within 48 hours**) report the following to the human subject research program manager:

- Any significant adverse events, unanticipated risks, and complaints about the research, with a description of any corrective actions taken or to be taken
- Any suspension or termination of IRB approval of research
- Any significant non-compliance with HRPP procedures or other requirements
- Any compromise of personally identifiable information must be reported immediately (as soon as the breach is discovered)

3.5 Department of Education (ED)

When research is supported by the Department of Education, USC fulfills its obligations with regard to the assurances and certification required by 34 CFR Sections 97 Subpart D (equivalent to 45 CFR Section 46 Subpart D), 24 CFR Section 356.3 and 34 CFR Section 99. The specific requirements for research supported by the Department of Education are listed below.

Access to Instructional Materials Used in Human Subjects Research

- All instructional material – including teachers' manuals, films, tapes, or other supplementary instructional material – which will be used in connection with any research or experimentation program or project must be available for inspection by the parents or guardians of the children engaged in such research.
- Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

- Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.

3.6 State Laws that Apply to Human Subjects Research

In addition to federal regulations [45 CFR 46](#) and Food and Drug Administration (FDA) regulations [21 CFR 50](#), [56](#), researchers are also expected to follow state and local laws. In California, there are additional state laws applicable to human subjects research. It is the responsibility of the Institution and researchers to know and follow these laws. Visit the [Official California Legislative Information](#) website to access California Codes.

Investigators and IRB personnel with questions regarding how state or federal regulations apply to a specific research project should contact the Chair of the IRB and/or the Office of Compliance. Additional options include seeking guidance or interpretation from the USC Office of General Counsel. Final interpretation and expectations with respect to California law reside with the Office of Compliance, and Office of General Counsel at USC.

The California Protection of Human Subjects in Medical Experimentation Act ([Section 24170-24179.5](#)) requires all medical experimentation to be “undertaken with due respect for human life and the right of individuals to determine what is done to their own bodies”.

A “medical experiment” is defined (section 24174 California Health and Safety Code) as follows:

- The severance or penetration or damaging of tissues of a human subject or the use of a drug or device, as defined in Section 109920 or 109925, electromagnetic radiation, heat or cold, or a biological substance or organism, in or upon a human subject in the practice or research of medicine in a manner not reasonably related to maintaining or improving the health of the subject or otherwise directly benefiting the subject
- The investigational use of a drug or device as provided in Sections 111590 and 111595

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- Withholding medical treatment from a human subject for any purpose other than maintenance or improvement of the health of the subject

All subjects participating in a medical experiment must be provided a written “experimental subject’s bill of rights” in addition to informed consent. Refer to [Section 10.11 – California Experimental Subject’s Bill of Rights](#) for additional information.