CHAPTER #1: Complete Necessary Training

UC Davis conducts research studies according to FDA regulations and ICH guidelines. Standardized training and continuing skill development of all clinical research professionals is an important part of preparation for clinical research. It is the responsibility of all staff and investigators to know, understand, and maintain sufficient knowledge of the federal, state, and local requirements protecting research participants.

1.1 Become Aware of Laws Governing Clinical Research

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1.1.1 Department of Health and Human Services (HHS)

HHS is the government’s principal agency for protecting the health of all Americans. It comprises several public health services agencies including the FDA (Food and Drug Administration), OHRP (Office of Human Research Protection), the NIH (National Institutes of Health), and the Centers for Medicare and Medicaid Services (CMS).

**Food and Drug Administration (FDA)** is responsible for protecting and promoting public health through the regulations and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), veterinary products, and cosmetics ([www.fda.gov](http://www.fda.gov)). Understanding these rules is critical for any investigator who conducts human subject studies with drugs, devices or dietary supplements, whether already approved on the market or still investigational, including new uses of approved products.

**Office of Human Research Protection (OHRP)** provides leadership, guidance, and education in the protection of the rights, welfare, and well-being of subjects involved in research conducted or supported by the HHS. OHRP performs these services through providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight, and providing advice on ethical and regulatory issues in biomedical and social-behavioral research. Detailed regulations for human subject protection are listed on the OHRP website ([http://www.hhs.gov/ohrp](http://www.hhs.gov/ohrp)). OHRP rules guide the Institutional Review Boards (IRBs).

**National Institutes of Health (NIH)** seeks to provide fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability. As part of this mission NIH provides leadership and direction to programs designed to improve health and provides support for research ([www.nih.gov](http://www.nih.gov)).
Currently, more than 50 medical research institutions in 31 states and the District of Columbia receive CTSA Program funding. These institutions are working together to speed the translation of research discovery into improved patient care. The CTSA program has the following overriding objectives:

1. Provide a comprehensive array of essential tools and services to spark clinical and translational research.
2. Ensure the training of a well prepared workforce of trainees, staff, and investigators.
3. Effectively communicate the many tools, services, and training opportunities to ensure innovative translational science advances that will improve human health.

Today, the UC Davis CTSC ([www.ucdmc.ucdavis.edu/ctsc](http://www.ucdmc.ucdavis.edu/ctsc)) offers a robust array of resources that faculty, trainees, and staff across the scientific and medical spectrum can use to enhance research and improve health and health-care delivery. The Clinical Trials Resource Group, author of this guidebook, is a program at the UC Davis CTSC.

**Centers for Medicare and Medicaid Services (CMS)** is the US Federal agency which administers Medicare, Medicaid, and the Children’s Health Insurance Program ([www.cms.gov](http://www.cms.gov)). On June 7, 2000, the President of the United States issued an executive memorandum directing the Secretary of Health and Human Services to “explicitly authorize [Medicare] payment for routine patient care costs…and costs due to medical complications associated with participating in clinical trials.” CMS responded to the executive order with the clinical trial policy - National Coverage Determination (NCD). Medicare State fiscal intermediaries also issue Local Coverage Determinations (LCD). As of August 2013, California’s intermediary is Noridian. Understanding Coverage Rules is critical for generating correct billing claims for clinical research participants. In 2013 the Affordable Care Act strengthened the provision for insurance coverage for individuals participating in clinical trials. Insurers will be prohibited from dropping or limiting coverage because an individual chooses to participate in a clinical trial. This applies to all clinical trials that treat cancer or other life-threatening diseases.

At UC Davis, the tool and the process of applying CMS rules to each individual study is called Coverage Analysis. This information is reviewed in detail in Chapter #6 of this Guidebook.

### 1.1.2 Code of Federal Regulations

The Code of Federal Regulations ([CFR](https://ecfr.gpoaccess.gov)) is a compendium of the general and permanent rules and regulations published in the Federal Register by the federal executive departments and agencies. The CFR is divided into 50 titles that represent broad areas subject to Federal regulations. Title 45 CFR encompasses regulation of Public Welfare. Title 21 CFR is administered by the FDA and covers regulations of Food and Drugs (as well as medical devices, biologics, vaccines etc.).

**Title 45 CFR 46 (The Common Rule)** is a core set of regulations defining protection of Human Subjects in clinical research. 45 CFR part 46 includes four subparts: subpart A, also known as the Federal Policy or the “Common Rule”; subpart B, additional protections for pregnant women, human fetuses, and neonates; subpart C, additional protections for prisoners; and subpart D, additional protections for children. Through a system of IRB registration and assurances, HHS regulations require institutions to commit to compliance with 45 CFR 46 before initiating participation in HHS-conducted or -supported research involving human subjects.
The main elements of the Common Rule include:

What human research issues are addressed in 45 CFR part 46?
(adapted from answers.hhs.gov)

HHS regulations at 45 CFR part 46 stipulate substantive and procedural requirements for investigators and institutions engaged in HHS-supported or -conducted research. Specifically, in addition to providing definitions and information about application of the regulations, specific sections of the regulations address the following topics:

- Assuring compliance with the regulations (46.103)
- Institutional Review Board (IRB) membership (46.107)
- IRB functions and operations (46.108)
- IRB review of research (46.109)
- Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research (46.110)
- Criteria for IRB approval of research, including minimizing risk, ensuring confidentiality, and protecting vulnerable populations, (46.111)
- Review by institution (46.112)
- Suspension or termination of IRB approval of research (46.113)
- Cooperative research (46.114)
- IRB records (46.115)
- General requirements for informed consent (46.116)
- Documentation of informed consent (46.117)
- Applications and proposals lacking definite plans for involvement of human subjects (46.118)
- Research undertaken without the intention of involving human subjects (46.119)
- Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency (46.120)
- Use of Federal funds (46.122)
- Early termination of research support: Evaluation of applications and proposals (46.123)
- Conditions (46.124)

Additional protections for specific populations have been adopted by HHS (and other departments and agencies to a lesser extent), as follows:

- Subpart B, Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
- Subpart C, Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- Subpart D, Additional Protections for Children Involved as Subjects in Research
As written, 45 CFR 46 applies only to federally supported research. However, most universities, including UC Davis, maintain an agreement called the Federalwide Assurance (FWA) with HHS that extends the protections of 45 CFR 46 to all research conducted by University personnel, regardless of the source of funding, or lack thereof. The FWA is required before the institution may receive federal research funds. UC Davis’ Federalwide Assurance Number (FWA#) is 00004557, and is approved up to June 28, 2016.

Since 1991, 45 CFR Part 46 was formally adopted by more than a dozen other Departments and Agencies that conduct or fund research involving human subjects.” The Department of Veterans Affairs promulgated this same rule at 38 CFR Part 16. Today, this Federal Policy is shared by 17 Departments and Agencies, representing most, but not all, of the federal Departments and Agencies sponsoring human-subjects research.

**Title 21 CFR**

The FDA regulations (Title 21 CFRs) are applicable when research is being conducted to develop a medical product that will be licensed for sale in the United States. Certain federally sponsored and privately sponsored research is subject to the regulations of the FDA according to 21 CFR Parts 50 and 56. Title 21 CFR part 50 defines regulations for informed consent and 21 CFR part 56 defines regulations for IRBs. These regulations largely overlap but are not identical with the Common Rule. Investigators need to know both sets of regulations to apply them appropriately.

Title 21 CFR 312 details the regulations for human research done with investigational drugs. This Title includes, but is not limited to, the regulations for applying to FDA to conduct research under an Investigations New Drug (IND) application (21 CFR 312 Subpart B), responsibilities of Sponsors and Investigators under an IND (21 CFR 312 Subpart D), and expanded access to Investigational Drugs (21 CFR 312 Subpart I). Activity#3 of this Guidebook discusses the drug development process in more detail.

Title 21 CFR 812 details the regulations for human research with investigational devices. The regulations lay out the framework for applying to FDA to conduct human subjects research with Investigational Devices (21 CFR 812 Subpart B), responsibilities of Sponsors (21 CFR 812 Subpart C) and Investigators (21 CFR 812 Subpart E), and IRB approval 21 CFR 812 Subpart D). Activity#3 of this Guidebook discusses the device development process in more detail.

**1.2 Read UC Davis Clinical Research Guidebook (current edition)**

The UC Davis Clinical Research Guidebook is updated on an annual basis to provide updates and new information. Always reference the most recent edition.


**1.3 Read Clinical Trials SOPs housed by CTSC**

The CTSC creates and maintains multiple SOPs related to conduct of clinical research at UC Davis. These SOPs can be found on the Clinical Trials website. For convenience, the same website houses links to IRB SOPs and UCDHS policies and procedures: [http://intranet.ucdmc.ucdavis.edu/ctsc/area/clinicaltrials/sops/index.shtml](http://intranet.ucdmc.ucdavis.edu/ctsc/area/clinicaltrials/sops/index.shtml)
As of date of publication, CTSC promulgated the following SOPs:

SOP#1 Training and Development Requirements (updated 02/08/2012)
SOP#2 Roles and Responsibilities of the Research Team (updated 02/08/2012)
SOP#3 CTSC Mentoring Program for CRCs (updated 03/14/2013)
SOP#4 Coverage Analysis (updated 05/8/2014)
SOP#5 Budget Approval for Industry Initiated Studies (updated 03/14/2013)
SOP#6 Development of Clinical Trial Budgets for Grant Proposals (updated 05/8/2014)
SOP#7 Financial oversight of clinical trials (updated 09/2012)
SOP#8 Completing an Internal Industry-Sponsored Clinical Trial Budget (updated 03/13/2013)
SOP#9 Principal Investigator Effort Reporting (updated 4/2012)
SOP#12 Medicare Advantage Plan Research registration (updated 6/14/2012)
SOP#13 Create and Manage research Studies in EMR/Epic (updated 05/08/2014)

1.4 CITI Training

UC Davis employs the Collaborative Institutional Training Initiative (CITI) program—a web based training program to satisfy the training requirements for all personnel conducting human subject research at UC Davis. CITI offers two versions of the Basic Human Research Training course: one for Biomedical Investigators and one for Social & Behavioral Investigators. A module on good clinical practice (GCP) is also required for individuals conducting clinical trials. Certification is valid for 3 years. For more information, please see http://research.ucdavis.edu/c/cs/hrp/res/roe

1.5 UCDHS Mandatory Annual Training

This is the annual safety training and code of conduct required for all UC Davis Health System employees as required by The Joint Commission, State of California, Department of Public Health and UC Davis Health System Hospital Policy 2903. For more information, please see http://www.ucdmc.ucdavis.edu/cppn/mat

1.6 UCDHS Privacy and Security Training

The objectives of the training are to understand what information must be protected under State and Federal privacy laws, including understanding patient's rights as it relates to the access, use and disclosure of their medical information. It also addresses individual responsibility in protecting health information and the consequences of non-compliance. For more information, please see http://www.ucdmc.ucdavis.edu/compliance/Quiz/PrivacySecurity/player.html

1.7 Dangerous Goods Shipping for Infectious Substances and Dry Ice

The Dangerous Goods shipping course is only offered online. Documented training is required every two years, based on the current edition of the International Civil Aviation Organization Technical Instructions for the Safe Transport of Dangerous Goods by Air (ICAO TI). The Saf-T-Pack training (https://www.training.saftpak.com) is compliant with the various national and international regulations, including IATA DGR, Transport Canada TDGR, US Department of Transportation 49 CFR and the European Agreement concerning the International Carriage of Dangerous Goods by Road and by Rail (ADR/RID).

To access the online training, please send an email to Diane Hoffmann dehoffmann@ucdavis.edu
An activation code, unique for each student, will be sent to you along with instructions to access the current training. Each student creates their own password.

1.8 Lab Safety Training or Biological Safety, Chemical/Laboratory Safety, and Hazardous Waste Management and Minimization

The Lab Safety training is geared toward School of Medicine employees. UC Davis Safety Services on the Main Campus offers numerous Instructor-led and online courses [http://safetyservices.ucdavis.edu/tr/lmsL]. If you are a UCDHS employee and involved in specimen processing, you may attend the Lab Safety training offered by Diane Hoffman. Regardless of their work location, all UCDHS employees involved in specimen processing are required to complete the following suite of classes.

1. UC Laboratory Safety Fundamentals (Safety Services only)
2. Bloodborne Pathogen Awareness (Safety Services and UCHDS),
3. UC Davis Biosafety Level 2 Online Training (Safety Services and UCHDS),
4. Proper Handling of Materials at Biosafety Level 1 (Safety Services and UCHDS)
5. Fume Hood Training (satisfied by completing #1 above)
6. Safe Use of Biological Safety Cabinets (Safety Services only)
7. Before You Sign the Hepatitis B Declination (Safety Services and UCHDS).

The on-line Laboratory Safety Fundamentals is required **every three years**. All other training can be fulfilled by attending UCDHS Instructor-led Lab Safety Training as the initial training. Laboratory Safety training dates are posted on: [http://www.ucdmc.ucdavis.edu/medresearch/medsp/labsafety.html](http://www.ucdmc.ucdavis.edu/medresearch/medsp/labsafety.html)

After the initial training, please document that each person has read, signed and dated the Prevention Plans as required by their occupation.

1. Department Injury & Illness Prevention Plan (IIPP). This Plan contains Job Safety Analysis that should be completed and kept on file at the Department for the duration of the employment.
2. Emergency Action Plan (EAP),
3. Biological Use Authorization (BUA),
4. Bloodborne Pathogen Exposure Control Plan (BBPECP),
5. Medical Waste Management Plan (MWMP),
6. Chemical Hygiene Plan (CHP) – within UC Davis Laboratory Safety Manual

The Plans and a template of the Employee Training Attendance Records can be found on:


1.9 IRB New Submitter and In-Service Training

New Submitter Training is conducted by the IRB Administrations Outreach, Training and Education team. This orientation provides detailed training on the ethical principles of human research, an explanation of the researcher’s primary responsibility for protecting research subjects and for
complying with all applicable provisions of institutional, state and federal laws. It provides an explanation of the different levels of IRB review and describes the processes for IRB submissions.

For more information, please see [http://research.ucdavis.edu/policiescompliance/irb-admin/outreach/](http://research.ucdavis.edu/policiescompliance/irb-admin/outreach/)

In addition, an Investigator Manual, Standard Operating Procedures, and a Human Research Protection Program Plan are available as guides for the policies and procedures related to the conduct of Human Research that are specific to UC Davis. The document discusses the mechanics of working with the IRB and Human Research Protection Program.


**1.10 CTSC Clinical Trials Education and Training Program**

The UC Davis Clinical Trials Resource Group, a CTSC program, makes education and training outreach a high priority. The curriculum delivers practical knowledge for GCP implementation on site. Information delivery is structured in three tiers: 1) general information about what is new in the clinical research arena, 2) information pertinent to UC Davis-specific knowledge areas and 3) in-depth training on UC Davis processes and procedures. The program delivers information via the following formats: web-based seminars and monthly updates, in-service and small group training, one-on-one mentoring program, a blog, Clinical Trials Newsletters, the UC Davis Clinical Research Guidebook, several process maps and checklists, and a comprehensive Clinical Trials website.

Monthly newsletters contain short informational articles with policy changes, process clarifications and announcements. The same information is presented during the monthly teleconferences, accompanied by power point presentations and live demonstrations. Clinical Research Process Maps, a visual step-by-step guide, are designed to assist with navigation of clinical trials administrative processes in an easy to follow, at-a-glance format. Separate Process Maps are created for Interventional Trials, Non-Interventional Studies [i.e., chart reviews] and Social-Behavioral Studies. A Supplemental Checklist bridges the Guidebook and Process Maps and serves as a tool for those who wish to visually track their progress through the administrative landscape. These tools are required reading for new clinical research coordinators entering the CRC Mentoring program. Investigators and staff can attend the monthly Clinical Trials Brown Bag seminars featuring content experts from around the country addressing new developments in clinical research. CRC Introductory 1.0 and CRC Basic 2.0 courses allow small groups of coordinators to study the best practices for GCP implementation on site in depth.

For more information, please see [http://www.ucdmc.ucdavis.edu/clinicaltrials/Training/](http://www.ucdmc.ucdavis.edu/clinicaltrials/)

**1.11 CRC Mentoring Program**

Investigators are responsible to ensure that new staff members are qualified to participate in clinical research based on their education and training. If the Department/Center is unable to provide an adequate mentoring or training support, the CTCS Mentoring Program can provide this service.
The CTSC CRC Mentoring Program is a one-on-one mentoring program for UCD Clinical Research Coordinators and other research staff in a CRC function role. Clinical Research Coordinators and research staff that function in a CRC role are able to participate at the discretion of their home Departments/ORUs. Selection of staff for the program is prioritized for those participating in FDA-regulated clinical trials with drugs, devices or dietary supplements. The program is provided for a maximum of 10 hours of face-to-face training with a CTSC mentor. Department funding is required for the trainee to enter the program.

Mentoring Program Goals:
- Expand knowledge of resources for clinical trials education and training
- Provide individual personalized mentoring based on the mentee’s level of skills, knowledge and experience.

Mentee’s Goals:
- Assess current level of skills and knowledge
- Receive personalized education and training plan
- Receive hands-on training for selected areas of core expertise
- Increase comfort level in job responsibilities

For more details, see CTSC SOP#3 and http://www.ucdmc.ucdavis.edu/clinicaltrials/Training/Mentoring.html

1.12 In Service Trainings: Coverage Analysis and Internal Budgets

In-Service training is available for both Coverage Analysis and internal budgets. For more information contact Suzan Bruce (916-703-0120) or Julie Calahan (916-734-2547).

Also see http://intranet.ucdmc.ucdavis.edu/researchbudgeting/index.shtml (internal)

1.13 Financial Conflict of Interest training

On August 24, 2012, new and more stringent rules for the disclosure of financial interests took effect for all research sponsored by the Public Health Service (PHS), including the National Institutes of Health (NIH). The new rules also apply to several non-federal sponsors, including the American Cancer Society and the American Heart Association. A list of agencies and entities (“covered entity”) that have adopted the PHS financial conflict of interest (FCOI) and disclosure rules can be found at:


The FCOI rules apply to all “investigators” who engage in any research funded by a covered agency. “Investigators” are defined by PHS to include principal investigators and any other individual who, regardless of title or position, have responsibility for the design, conduct, or reporting of such covered research. This includes, for example, any graduate student or post-doctoral fellow who meets the definition of investigator.
Each investigator must separately submit to the Institution (UC Davis’ Research Compliance and Integrity) a financial disclosure statement. The Disclosure must identify financial interests of the investigator, spouses/registered domestic partners, and dependent children that exceed the thresholds set by PHS and relates to any of the investigator’s institutional responsibilities.

Disclosures must be made: (1) prior to the Notice of Award issue date for additional funds if you are already conducting covered research as of August 24, 2012; (2) no later than at the time of application for funding from a covered agency if the application is submitted after August 24, 2012; (3) annually; and (4) within 30 days after acquiring or discovering a financial interest that must be disclosed as defined by PHS.

In addition, all investigators who are engaged in any research funded by a covered entity as of August 24, 2012 must complete mandatory training prior to the receipt of any new funds from the covered entity via a Notice of Award. Any investigator who is added to an existing research project after August 24, 2012 must complete the training prior to engaging in any research on the project.

Both COI Mandatory Training and Mandatory Disclosure form can be found on Research Compliance and Integrity Website: http://research.ucdavis.edu/policiescompliance/coi/phs/

1.14 UCDHS Mandatory Epic® EMR Clinical Research Management eLearning

On behalf of the Health System Compliance department, it is mandatory for all Principal Investigators to complete the 10 minute Epic Research Management eLearning designed specifically for Investigators. UC Learning Center (lms.ucdavis.edu) course is # 08084.

It is also mandatory for all Clinical Research Coordinators or any staff in functional CRC role (i.e., Research Nurse, Research Associate etc.) to complete the 10 minute Epic Research Study Management elearning. UC Learning Center (lms.ucdavis.edu), course is # 08074.

For more information see EMR research website: http://intranet.ucdmc.ucdavis.edu/emr/projects/P_New_Dest/Research.shtml