1. HIPAA Privacy Rule
2. Clinical Trials Billing
3. Conflict of Interest Related to Research
4. Confidentiality Agreements and Clauses
USC’s Office of Compliance is charged with helping USC faculty and staff employees understand and comply with laws, rules, and regulations applicable to their work, preventing and detecting violations of law, regulations, and university policy, and promoting ethical conduct, as articulated in the USC Code of Ethics. To accomplish this charge, the Office of Compliance:

- Performs periodic risk assessments;
- Assists in the development of standards, policies, and procedures to prevent and detect violations;
- Provides training and education on ethical standards, policies, and procedures;
- Conducts periodic assessments, monitoring and auditing; and
- Investigates allegations of non-compliance and recommends corrective action where appropriate.

The Office of Compliance also oversees USC’s Help and Hotline, (213) 740-2500. USC faculty, staff, and students can call this number to ask questions about applicable laws, regulations and university policies that may impact their job duties. The Help & Hotline also can be used to confidentially report suspected violations of law, regulation or policy without fear of retribution.

For research coordinators who support the design and conduct of clinical trials, it is important to be familiar with several laws and USC policies, many of which are also found elsewhere in this manual. In this section, we will focus on four areas:

- HIPAA Privacy Rule
- Clinical Trials Billing
- Conflicts of Interest Related to Research
- Confidentiality Agreements and Clauses

**HIPAA PRIVACY RULE**

The USC Code of Ethics calls for a commitment to respecting the rights and dignity of all persons. Part of this commitment involves protecting the rights of individuals in safeguarding and keeping confidential a person’s health information. In addition, the Health Insurance Portability and Accountability Act (also known as HIPAA or the HIPAA Privacy Rule) is a federal law that establishes minimum standards for safeguarding the privacy of an individual’s Protected Health Information (PHI), which is defined as individually identifiable health information transmitted in any form or medium.

These protections are related to but distinct from those provided through the informed consent process. In the informed consent process, patients or healthy (“normal”) volunteers make an informed and voluntary decision about whether to participate in a research study based on the study’s risks and benefits. The HIPAA Privacy Rule provides additional protection related to the privacy and security of PHI obtained in the course of conducting research.

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COMPLIANCE: CONSIDERATIONS RELATED TO CLINICAL TRIALS

The Privacy Rule provides several methods by which a human subject’s health information may be obtained in connection with a research study:

Generally, researchers must obtain a written HIPAA Authorization from human subjects (in addition to informed consent) when conducting a research study using PHI. The HIPAA authorization allows a researcher to use PHI for specified research purposes (not including treatment, payment, or health care operations), or to disclose PHI to a third party specified by the individual. A copy of USC’s HIPAA Research Authorization template can be found at [http://policies.usc.edu/p2admOpBus/hipaa.html](http://policies.usc.edu/p2admOpBus/hipaa.html).

A HIPAA Waiver or Alteration of the authorization requirement allows researchers to use or disclose PHI without obtaining authorization from subjects as long as certain criteria are met:

- The PHI will be protected from improper use and disclosure;
- Identifiers will be destroyed at the earliest opportunity consistent with the conduct of research;
- PHI will not be reused or disclosed to any other person or entity (except as required by law, for authorized oversight of the research study or for other research for which the use or disclosure of PHI is permitted by the Privacy Rule);
- The research could not practically be conducted without the waiver or alteration;
- The research could not practically be conducted without access to and use of the PHI.

The university’s Institutional Review Board (IRB) may approve a waiver or an alteration of the authorization requirement in whole or in part.

Preparatory to Research (or partial waiver) activities also allow researchers to access PHI as long as the researcher demonstrates that: access to PHI is only to be used to prepare a research protocol or for similar purposes preparatory to research; the PHI will not be removed from the covered entity in the course of review; and the PHI for which access is requested is necessary for the research.

The IRB is charged with ensuring that all researchers and their staff who need to access PHI are HIPAA compliant. In this capacity, the IRB will determine whether the research subject must sign a USC HIPAA Authorization (in addition to the informed consent form for the study), whether the authorization requirement can be waived, or whether authorization is not required. USC’s online iStar application ([https://istar.usc.edu](https://istar.usc.edu)) provides additional information about the circumstances when a waiver of HIPAA authorization may be appropriate.

Typically, at the time of enrollment, the subject signs the HIPAA research authorization and his or her informed consent. This enables the research team to obtain the health records that are covered by the authorization from the subject’s healthcare provider. It is critical for research coordinators to obtain a signed copy of the current, IRB-approved HIPAA authorization and maintain the authorization in a clinical trial/research binder so that it is available for inspection and audit.

The Office of Compliance must review and approve any changes to USC’s standard HIPAA research authorization template before the IRB will approve the protocol. Please send any proposed changes to the Office of Compliance for review.

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USC’s HIPAA Privacy and Security policies and procedures are available on the USC policies website at [http://policies.usc.edu/p2admOpBus/hipaa.html](http://policies.usc.edu/p2admOpBus/hipaa.html) or the USC Office of Compliance website at [http://ooc.usc.edu](http://ooc.usc.edu).

### Roles and Responsibilities of Research Coordinators

Working under the direction of the principal investigator:

- Ensure use of the most current version of the informed consent and HIPAA authorization forms as approved by the IRB for use in the study.
- Verify that a research authorization has been signed by each research participant.
- If there is no research authorization, determine whether the IRB has issued a waiver from the requirement to obtain a research authorization.
- Remember that a signed informed consent and a signed HIPAA authorization are generally necessary for every person enrolled in the study. A signed informed consent alone is not sufficient in a study requiring HIPAA authorization.
- Obtain HIPAA training.

### Case Studies

Both of the scenarios below are based on actual incidents, and highlight the importance of obtaining a written authorization that has been approved by the IRB.

**“Moved to Mexico”**

A USC researcher conducted a clinical trial on behalf of a major pharmaceutical company. During the course of the clinical trial, six subjects were enrolled. At the conclusion of the trial, the sponsor was reviewing the data gathered in preparation for an FDA submission and discovered that there was no authorization for one of the subjects, making it impossible for it to use that subject’s data as part of the FDA submission. Although the study team recalled obtaining an authorization from the subject, there was no documentation in the clinical trial folder to confirm that it had occurred.

In the course of the investigation, it was determined that the subject moved to Mexico. At considerable expense, efforts were undertaken to locate the subject, which were unsuccessful. Therefore, the sponsor could not use the data related to the subject and had to prepare revised documentation for its FDA submission.

**The case of the missing authorizations**

A year after nine subjects were enrolled in a clinical trial, it was determined that there were no research authorizations for any of the subjects. The subjects were enrolled for over a year before the discovery. After an investigation, it was determined that the informed consent and research authorizations were stapled together and the study coordinator did not realize that a separate signature was needed for both the informed consent and the research authorization.

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Efforts were undertaken to locate the enrolled subjects, but not all subjects could be located. As a result, data related to these subjects could not be used to support the findings of the research.

**CLINICAL TRIALS BILLING**

On a clinical trial, some costs for patient care may be billed to an insurer and some costs may be billed to the sponsor. However, it is inappropriate and unlawful to bill a particular cost (e.g., a lab test or procedure) to both the insurer and the sponsor, and certain costs may only be billed to the sponsor.

In 2000, the Centers for Medicare and Medicaid Services (CMS) issued a national coverage determination (NCD) for clinical trials that defined which costs are billable to Medicare. Under the NCD, Medicare will only pay for routine patient care costs, certain research costs, and costs due to complications associated with participation in qualifying clinical trials. USC follows these same standards for all insurers. It is essential for USC to do so because violations might subject the university to fines under the False Claims Act.

To meet its obligations under the NCD, USC, through its Clinical Trials Office (CTO), conducts an assessment called a Medicare Coverage Analysis (MCA) to determine which activities to be undertaken in connection with a clinical trial may appropriately billed to insurance and which must be billed to a research sponsor. Generally speaking, the process for making this assessment is as follows:

- The PI/Study Coordinator notifies the Clinical Trials Management Team (CTM) within CTO that the PI is initiating a new research project. As part of the notification, the PI/Study Coordinator forwards to the CTO team all essential documents related to the clinical trial, including:
  - The protocol;
  - Investigational drug/device brochure;
  - Draft clinical trial agreement (CTA);
  - Sponsor’s proposed draft budget;
  - Laboratory manual;
  - Investigational New Drug (IND)/Investigational Device Exemption (IDE) letter;
  - Names of research personnel involved in the study and hourly/administrative rates.

- CTO reviews the protocol and sponsor’s budget and other related documents and assesses which costs associated with the trial are “routine patient care costs” and which are not.
- The completed MCA analysis is used to develop a counter-proposal to the sponsor’s proposed draft budget. CTO then negotiates with the sponsor and finalizes the research agreement and associated budget.
- Once the budget is finalized, a Research Order Form (ROF) is generated that is used for ordering all research-related tests and procedures. The ROF indicates which services should be paid by insurance, and which should be billed to a USC research account. If a service is not billable to insurance, it must be charged to a research account identified on the ROF. In some rare
instances the cost may be charged to the subject, but this must be noted on the informed consent.

- After the study commences, the research coordinator notifies Sponsored Projects Accounting (SPA) each time he or she enrolls a new study subject for the trial so that the subject can be entered into the TRUE 2 system and all services can be billed properly, consistent with the approved budget. As part of this notification, the research coordinator provides a copy of the signed informed consent and HIPAA research authorization to SPA.

Roles and Responsibilities of Research Coordinators

- Assist the PI in developing study-related documents as part of the initiation of a new clinical trial;
- Notify CTO within 24 hours of enrolling all new subjects in the trial. Coordinators should be sure to include a copy of the signed informed consent and HIPAA research authorization as part of the notification;
- Use the Research Order Form from TRUE 2 to schedule all services for each subject.

CONFLICT OF INTEREST IN RESEARCH

USC encourages its faculty, staff and students to participate in meaningful professional relationships with industrial and other private partners. These partnerships are established for mutually beneficial reasons and many times produce knowledge and technology that will help to meet societal needs.

In certain circumstances, relationships with outside interests can create, or appear to create, conflicts of interest. While having a conflict of interest does not imply wrongdoing or inappropriate activity, conflicts do require prompt disclosure so that they can be reviewed and managed to ensure that the conflict does not improperly influence, or appear to improperly influence, how USC research is proposed, conducted or reported.

Conflicts of interest are governed by several USC policies:

- **Conflicts of interest in research**, pertaining to personal interests that pose a potential conflict related to research;
- **Institutional conflicts of interest in research**, pertaining to potential research-related conflicts created by USC’s financial interests, such as its investments;
- **Relationships with industry**, pertaining to financial interests of health care providers with the pharmaceutical or medical device industry, whether or not those interests relate to research or create a conflict of interest;
- **Conflicts of interest in professional and business practices**, pertaining to personal considerations that may compromise, or have the appearance of compromising, an individual’s professional judgment and ability to perform his or her responsibilities to USC.

With respect to conflicts of interest in research, researchers must disclose the following types of outside activities and financial interests when held in a research sponsor or outside entity that has an economic interest in the outcome of research, regardless of sponsor:
• Payments for service (consulting payments, payments for service on a board or advisory committee, paid authorship) in excess of $5,000 a year;
• Private equity interests (e.g., stocks, stock options or other ownership interests not publicly traded), regardless of value;
• Public equity interests of $5,000 or more (except when held in an investment vehicle like a mutual fund);
• Management roles (e.g., director, officer, or similar position of significant decision-making authority).

Conflicts of interest that relate to human subjects research are scrutinized more closely than other conflicts, making it particularly important to identify and disclose any such conflicts as promptly and thoroughly as possible.

Conflicts of interest must be disclosed via USC’s on-line conflict disclosure system, “diSClose” (https://disclose.usc.edu) by the person holding the conflict (i.e., an investigator can never delegate responsibility to disclose his or her own conflict to a research coordinator). diSClose is the system for disclosing potential conflicts of all types, under all conflict policies. In addition to disclosing the conflict in diSClose, conflicts must be indicated in iSTAR.

Roles and Responsibilities of Research Coordinators

• Encourage investigators to promptly disclose any outside relationships related to research in the diSClose system;
• Ask the investigator to complete the portion of the iStar submission that asks whether a conflict exists, and do not answer this question unless the investigator has affirmed in writing whether or not a potential conflict exists;
• When a management plan requires that informed consent be obtained by someone other than the investigator, help ensure that plan is followed;
• Inform the principal investigator when your financial interest poses a potential conflict.
• Disclose your financial interests through diSClose when it poses a potential conflict on a research study, and comply with any management plan put in place to manage the conflict;
• Complete on-line training on conflicts of interest in research.

CONFIDENTIALITY AGREEMENTS AND CLAUSES

A researcher’s work may involve acceptance of confidential or proprietary information, materials, software code, or technology from a sponsor or third party, which may include:

• Protocols, investigator’s brochure and written instructions;
• Information that is not published;
• Oral disclosures of confidential information;
• Data from the study.

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Confidential information generally does not include information that is publicly known or known prior to receipt of information from the outside party, and does not include medical records of the patients and investigators’ personal notebooks.

In some cases, the university agrees to confidentiality through execution of a confidential data agreement (CDA) or non-disclosure agreement (NDA). Confidentiality requirements may also be contained in a clause within a clinical trial agreement (CTA), technology license, data sharing agreement, or material transfer agreement (MTA).

The CDA, NDA or agreement clause defines knowledge, information, or data that the parties wish to share and wish to restrict from wider use and dissemination. CDAs and NDAs are frequently used when the parties wish to enter into a sponsored research agreement and want to protect confidential information during the course of discussions. However, clinical trial agreements also typically contain confidentiality clauses that extend these provisions through the execution of the trial and beyond.

The CDA/NDA or clause may be a one-way (unilateral) agreement that requires only the receiving party to maintain secrecy. For example, a sponsor may provide information to a researcher so the researcher can determine if he or she would like to participate in a study. The CDA/NDA or clause may also be a two-way or mutual agreement in which both parties exchange confidential information and are obligated to maintain secrecy. Regardless of whether the agreement is unilateral or mutual, information provided to USC under the agreement cannot be disclosed to a third party.

At USC, the CTO and not the investigator reviews and signs CDA/NDA agreements related to the provision of confidential or proprietary information on clinical trials.

Access to confidential information must be limited to personnel who need the information to perform the study, work with patients or work with ancillary groups. The information should never be shared outside of USC, and should only be shared with others at USC if they need to know the information, and if they are informed that the information is confidential. Investigators and research coordinators alike are responsible for protecting confidential information.

Consult USC’s “Guide to Confidentiality” for further information.

Other confidential information related to clinical trials

Protected Health Information (PHI): In certain situations, sponsors may wish to provide USC identifiable health information protected by state and/or federal privacy laws. In connection with doing so, they may require the university to agree to meet various data privacy and security requirements with regard to the receipt, maintenance and use of such data. In the event you become aware that a sponsor is requiring the university to agree to data privacy/security standards associated with the provision of identifiable health information, please contact the Office of Compliance for assistance.

Certificates of Confidentiality: Certificates of Confidentiality are documents issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. Certificates of Confidentiality may be granted
for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. (i.e., sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information that, if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information or tissue samples). NIH Certificates of Confidentiality may also be authorized for studies not funded by NIH (i.e., NIH funding is not a condition for receiving a Certificate of Confidentiality).

For more information on Certificates of Confidentiality, including how to apply for and obtain one, please visit http://oprs.usc.edu/review/confident/.

**Roles and Responsibilities of Research Coordinators**

- Review the “Guide to Confidentiality” posted on the Clinical Trials @ USC website;
- Ask the research sponsor or principal investigator to identify confidential or proprietary information;
- Review restrictions associated with confidential or proprietary information that you may need to access or use, as reflected in the Clinical Trial Agreement;
- Assist the investigator in ensuring that necessary protections (i.e. data access and security) are in place with respect to confidential or proprietary information;
- Do not share confidential information with anyone outside USC, or anyone inside USC who does not need that information. When information must be shared, be sure to inform the recipient of its confidentiality and ensure that he or she is aware of the obligation to protect the confidentiality of the information;
- Contact the Office of Compliance for assistance if you are not sure whether confidential or proprietary information is being adequately protected.