

GUIDE TO CLINICAL RESEARCH AT USC



**Developed by the Office of Research
in collaboration with the following offices:**

*Office for the Protection of Research Subjects, Southern California
Clinical and Translational Science Institute (SC CTSI), Clinical
Investigations Support Office, Clinical Trials Unit, Office of Compliance*

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***<http://research.usc.edu>
<https://research.usc.edu/clinical-trials-at-usc>***

Congratulations! You have taken the initiative to educate yourself on the process of conducting studies involving human subjects at the University of Southern California. The purpose of this Guide is to provide you, the Principal Investigator, as well as your project managers, research and nurse coordinators or administrators, and all those associated with clinical trials, with an overview of the processes, committees and departments that you will work with throughout the submission, review, approval and conduct of your human subject study or clinical trial.

It also highlights important resources available to you at USC as you design and conduct your studies.

Significant efforts are currently being made at USC to streamline and improve our human subjects research protocol submission and approval process. This is a revised version of the original guide created in 2013.

We very much welcome and value your insights and experience – any comments or suggestions to improve upon our submission process can be submitted to Vprsch@usc.edu.

Randolph Hall
Vice President, Research



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I. UNIVERSITY ENTITIES & RESOURCES

1. Offices & Entities

- Keck School of Medicine (KSOM)
- LA County + USC Hospital
- Clinical Trials Office (CTO)
- Clinical Investigations Support Office (CISO)
- Office for the Protection of Research Subjects (OPRS)
- Institutional Review Board (IRB)
- USC Investigational Drug Services Pharmacy
- Southern California Clinical and Translational Science Institute (SC-CTSI)
- Office of Compliance (OOC)
- Sponsored Projects Accounting (SPA)

2. Ancillary Committees

- Institutional Biosafety Committee (IBC)
- Radiation Safety Committee (RSC)
- Stem Cell Research Oversight Committee (SCRO)
- Conflict of Interest Review Committee (CRIC)
- Clinical Investigations Committee (CIC)
- Quality Assurance Monitoring Committee (QAMC)
- Data and Safety Monitoring Committee (DSMC)
- Phase I Committee

3. Other Entities & Resources

- Cancer Center Database (CAFÉ)
- Research Facilities & Core Laboratories at USC
- Office of Research Administration (KSOM)
- USC Office of Research
- Department of Contracts and Grants (DCG)
- USC Stevens Center

1. OFFICES AND ENTITIES

This chapter provides an overview of the offices, entities and ancillary committees at USC associated with Human Subject Research (HSR). The scope of activities encompassed by HSR is very broad and includes scientific, investigatory and research activities involving human subjects, clinical data, or any materials (including tissues, serum, cells, and DNA) from any human source, whether specimens are from a known, specified individual or are "de-identified."

KECK SCHOOL OF MEDICINE (KSOM)

Established in 1885 and located at the Heath Science Campus (HSC), the [Keck School of Medicine](#) is the oldest medical school in Southern California and is home to the Keck Medical Center, which is composed of three USC-owned hospitals:

- [Keck Hospital of USC](#) (formerly USC University Hospital) is a private research and teaching hospital staffed by more than 500 physicians who are also faculty of USC's Keck School of Medicine. The hospital's 18 [departments](#), individual [clinical programs](#) and integrated clinical and business services provide support to USC's academic physicians.
- [USC Norris Comprehensive Cancer Center and Hospital](#), a 60-bed inpatient facility, features a bone marrow transplantation unit and a surgical unit exclusively designated to cancer research and patient acute and critical care.
- [USC Verdugo Hills Hospital](#) is a 158-bed hospital in Glendale staffed by USC faculty physicians. Services include a 24-hour emergency room, a primary stroke center, bariatric and minimally invasive surgery, OB-GYN and infant services, orthopedic surgery, occupational, physical and speech therapy, cardiac rehabilitation, and imaging and diagnostic services including mammograms, magnetic resonance imaging (MRI), CT scans and angiograms.

In addition, the Department of Pediatrics of [Children's Hospital, Los Angeles \(CHLA\)](#) is the largest department within the USC Keck School of Medicine. CHLA has been affiliated with KSOM since 1932. CHLA's Department of Pediatrics is composed of [20 divisions](#), including [bone marrow transplant](#) and a [pediatric intensive care unit](#). Their Department of Surgery is one of the country's most comprehensive, encompassing [nine divisions](#), including five solid organ transplant programs (heart, lung, liver, intestine and kidney). In 1992, the CHLA Research Institute became the [Saban Research Institute](#), which houses over 150,000 sq. ft. of research space and provides investigators with core facilities that include: molecular genomics/microarray, gene targeting and pathology, proteomics, biostatistics, Good Manufacturing Practice (GMP) in cell therapy, cellular imaging, fluorescence activation cell

sorting (FACS), stem cell, vector and research imaging. The hospital's The [Clinical Investigation Center](#) and the Clinical Trials Unit support clinical research while the [Office of Research Advancement and Administration](#) provides centralized support for all aspects of our research.

Additional KSOM research affiliates and medical centers include:

- [Healthcare Consultation Centers \(HCC\) 1, 2 and 4](#)
- [House Ear Institute](#)
- [Keck Medicine of USC Downtown Los Angeles](#)
- [Keck Medicine of USC – Beverly Hills](#)
- [Keck Medicine of USC - Glendale](#)
- [Keck Medicine of USC – La Cañada Flintridge](#)
- [Keck Medicine of USC - Pasadena](#)
- [Outpatient Surgery Center](#)
- [USC Center for Childhood Communication](#)
- [USC Engemann Student Health Center](#)
- [USC Norris Oncology/Hematology Irvine](#)
- [USC Norris Oncology/Hematology Newport Beach](#)
- [USC Norris Treatment Center Newport Beach](#)
- [USC Norris Westside Cancer Center](#)
- [USC Surgery - Glendale](#)
- [USC Urology - Bakersfield](#)
- [Westside Center for Diabetes](#)

LA COUNTY + USC HOSPITAL (LAC+USC)

A partner institution of the Keck School of Medicine of USC, the [LAC + USC Medical Center](#) is one of the largest acute care hospitals in America, recording nearly 39,000 inpatient discharges, 150,000 emergency department visits, and 1 million ambulatory care visits each year.

LAC+USC provides a full spectrum of emergency, inpatient and outpatient services. These include medical, surgical and emergency/trauma services in the General Hospital. The Women's and Children's Hospital provides obstetrical, gynecological, pediatric and specialized neonatal intensive care services as well as psychiatric services for adults, adolescents and children. Staffed by USC faculty physicians, LAC+USC also operates one of only three burn centers in the county and is home to one of only a few Level III Neonatal Intensive Care Units in Southern California.

Research at LA County+USC Medical Center

USC research taking place at LAC+USC is subject to the **Sponsored Programs Agreement** executed in **December, 2014**. Here are some of the important provisions of the agreement:

Review by CMO and Research Committee: For all human subjects research, the IRB will submit the study protocol to the LAC+USC Chief Medical Officer (CMO) for review upon receipt, if the iStar application indicates research will take place at LAC+USC. The CMO is responsible for reviewing the protocol within 15 business days and sending a decision to the IRB as to whether LAC+USC will permit the research to take place. In the absence of a decision within 15 business days, approval will be deemed granted. Non-human subject research also requires review and approval by the CMO. In such cases the investigator should communicate directly with the CMO at least three (3) weeks prior to conduct of the study.

If the IRB application does not indicate the research will take place at LAC+USC, it will not be sent by the IRB to the CMO for review, and the study will not be approved to take place there.

Billing: LAC+USC will rely on the Medicare Coverage Analysis conducted by USC to determine which “research services, ancillary services and supplies” result from routine care (and are billable to insurance) and which services and supplies are non-routine (i.e., added expenses attributed to a research project). LAC+USC will bill Medicare and other third party payers directly for all routine care and will bill USC for all non-routine care.

Costs of Services and Supplies: LAC+USC bills according to rates approved by the LA County Board of Supervisors. These rates differ from Medicare rates, sometimes higher and sometimes lower. For federally sponsored studies, USC expects to be reimbursed at a rate equaling the minimum of the LA County rate and the Medicare rate. In instances where the LA County rate exceeds the USC rate, the difference will be charged to a departmental unrestricted account.

For industry sponsored studies, USC is in the process of establishing rates that accommodate both Medicare and LAC+USC rates.

These rates may be a factor in where you choose to conduct your research and are available for review from the CTO.

Research Order Forms: LAC+USC is developing a set of medical order forms, which will be required to request all research related services and supplies.

Records: In compliance with all applicable regulations and laws, the following information must be placed in each subject’s medical record: (1) copy of signed informed consent; (2) medical record note of enrollment; (3) list of any medications administered as part of the research, and

(4) notes needed for communication to the primary care provider to assure continued safe care. The agreement also requires reporting of adverse events to both the IRB and as applicable to LAC+USC's electronic reporting system. LAC+USC also requires reporting of names and medical record numbers of all enrolled subjects.

Attribution and Acknowledgment: Investigators should provide acknowledgment and attribution to LAC+USC in all scientific presentations and publications to the extent permissible.

CLINICAL TRIALS OFFICE (CTO)

The [Clinical Trials Office](#) supports USC's investigators through budgeting, conducting coverage analysis, contracting, and general sponsor relations for clinical trials sponsored by industry, government, and non-profit entities. CTO teams are composed of a **Senior Contract Manager** (reviews, negotiates, and executes the Clinical Trial Agreements, CTAs), a **Medicare Coverage Administrator** (conducts coverage analysis and helps with clinical trial budget development), and a **Budget Specialist** (develops a budget based on the coverage analysis and in a collaboration with the Principal Investigator). The CTO, through Sponsored Projects Accounting (SPA), also invoices sponsors for clinical research costs and reimburses providers (e.g., Keck Medical Center, research pharmacy, clinical trials unit) for costs of services and goods used in the research.

CTO Contact Information:

Phone: (323) 442-2396
E-mail: ctoffice@usc.edu

CLINICAL INVESTIGATIONS SUPPORT OFFICE (CISO), USC NORRIS COMPREHENSIVE CANCER CENTER (NCCC)

[CISO](#) serves as a centralized unit to oversee the clinical research infrastructure and assist investigators in their conduct of clinical trials and translational research projects. CISO has three main operational units:

- **The Protocol Administration Unit** provides the centralized consultation and regulatory services necessary for the design, initiation, and conduct of clinical trials.
- **The Protocol Implementation Unit** provides and manages staff for study conduct as well as oversight for quality assurance and data control.
- **The Administrative/Business Management Unit** fulfills administrative functions necessary for efficiency and coordination of CISO with sponsors, investigators and others.

CISO Contact Information:

Phone: (323) 865-0451
E-mail: CoreCISO@med.usc.edu

OFFICE FOR THE PROTECTION OF RESEARCH SUBJECTS (OPRS):

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;
- Investigates allegations of non-compliance and recommends corrective action where appropriate.

OPRS Contact Information:

Phone: (213) 821-1154
E-mail: oprs@usc.edu

As relevant to research coordinators, the Office of Compliance provides guidance on issues related to Privacy and Security, Conflicts of Interest, and Research Misconduct.

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. Please visit <http://ooc.usc.edu> for additional information.

INSTITUTIONAL REVIEW BOARD (IRB)

The Food and Drug Administration (FDA) defines IRB as any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects.

USC has IRBs at both the Health Science Campus ([Health Sciences Review Board – HSIRB](#)) and the University Park Campus ([University Park Institutional Review Board – UPIRB](#)). The former is charged with reviewing and overseeing primarily biomedical research projects submitted by students, faculty, or staff at HSC while the focus of UPIRB review is primarily socio-behavioral research projects submitted by students,

IRB Contact Information:

Health Science Campus
Phone: (323) 223-2340
E-mail: irb@usc.edu

University Park Campus
Phone: (213) 821-5272
E-mail: upirb@usc.edu

faculty, or staff at UPC. No human subject research can be conducted at USC without prior review and approval of the study protocol by the IRB.

USC INVESTIGATIONAL DRUG SERVICES PHARMACY

The Investigational Drug Services integrates its activities with the clinical, safety, informatics, administrative, and drug distribution systems of USC Hospitals and Clinics to optimize study drug therapy for patients. These services include: regulatory

compliance integrity of blinding; prevention of errors involving study drugs; dispensing of investigational products in a timely manner; contributing to study design and data integrity randomization; and providing drug and supply procurement, as needed, as well as study drug accountability, sterile preparation and distribution, of both hazardous and non-hazardous study medications in a USP 797-compliant environment. Research pharmacists also work with clinical investigators during clinical protocol develop, providing input on work flow processes, feasibility and budget.

Investigational Drug Services Contact Information:

Norris Cancer Center	(323) 865-3612
LAC-USC Hospital & Keck Hospital	
of USC's Ambulatory Clinics:	(323) 865-3538
Keck Hospital of USC:	(323) 442-8375

SOUTHERN CALIFORNIA CLINICAL AND TRANSLATIONAL SCIENCE INSTITUTE (SC-CTSI)

The [SC-CTSI](#) is one of 60 NIH-funded research institutes nationwide that aim to move discoveries through the research pipeline and into sustainable public health solutions. The institute provides USC clinical trial investigators with a range of research resources, from funding opportunities to mentorship and career development, including support with pre-clinical translation of discoveries; resources for community-engaged research; training and education; research team building activities, as well as expert advice/support in: biostatistics and bioinformatics, regulatory knowledge, study design and feasibility, data management and research ethics.

Clinical Trials Unit (CTU): The [CTU](#), part of the SC-CTSI, is an important resource for studies that require intensive pharmacokinetic (PK) and/or pharmacodynamic (PD) blood draws, as well as studies

that may require intensive monitoring (such as serial EKGs, etc.). The CTU is also equipped with a core laboratory that can perform complex specimen handling. It is suggested that investigators contact the CTU for all studies involving: (1) serial and frequent blood draws

CTU Contact Information:

Health Science Campus	(323) 865-3225
CHLA	(323) 361-5615

(beyond 2 or 3 draws that could be done in the day hospital or clinic); (2) serial blood draws for PD markers with complex specimen handling and/or (3) intensive monitoring with EKGs, vitals, etc.

OFFICE OF COMPLIANCE (OOC)

USC's [Office of Compliance \(OOC\)](#) 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:

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- 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;
- Investigates allegations of non-compliance and recommends corrective action where appropriate.

OOC Contact Information:

Phone: 213.740.8258
E-mail: complan@usc.edu

As relevant to research coordinators, the OOC provides guidance on issues related to Privacy and Security, Conflicts of Interest, and Research Misconduct.

The OOC 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. Please visit <http://ooc.usc.edu> for additional information.

SPONSORED PROJECTS ACCOUNTING (SPA)

Sponsored Projects Accounting ([SPA](#)) is charged with oversight of post award administration of sponsored research for the University, including: (1) managing awards for compliance with Federal, State, and Private agency fiscal and reporting guidelines, University policy and procedures, and with Generally Accepted Accounting Principles; (2) ensuring the payment of obligations and the collection of funds with an efficient cash management system and (3) encouraging and facilitating proper management of

SPA Contact Information:

<http://fbs.usc.edu/depts/spa/page/7708/clinical-trial/>

sponsored funds through training and development, streamlined financial systems, and high professional standards.

2. ANCILLARY COMMITTEES

As you develop and conduct a clinical or translational study, you will interact with several oversight committees at USC, some of which are specific to the Cancer Center for cancer-related studies.

INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)

The [Institutional Biosafety Committee](#) (IBC) reviews research use of all potentially hazardous biological agents including infectious agents, human and non-human primate materials (including established cell lines), known regulated toxins and carcinogens, select agents, recombinant DNA and studies involving human gene transfer. The committee is responsible for ensuring that research involving these agents is conducted in a manner that does not endanger the researcher, laboratory workers, human research subjects, the public or the environment. As an institution that receives NIH funding, the IBC must ensure that all research conducted at or sponsored by our institution complies with the [NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules](#).

IBC Contact Information:

E-Mail: IBC@caps.usc.edu

All clinical studies that include gene therapy and/or recombinant organism uses in human subjects must receive approval from the IBC in addition to IRB approval prior to study initiation. The submission of the Biohazardous Use Authorization form (BUA) is required, along with applicable documents, including the NIH Recombinant DNA Advisory Committee (RAC) Review letter, the clinical protocol, Responses to Appendix M of the NIH Guidelines, the informed Consent Form, the Investigator's Brochure, and any or all correspondence (e.g. RAC recommendations and response letters, approval letters, FDA correspondence, sponsor information or delegation, etc.). The IBC meets monthly.

To understand the scope of NIH requirements and the review process for human gene transfer trials, please see this link: http://oba.od.nih.gov/rdna/rdna_faq.html.

All studies that involve biohazardous materials must be registered with the [Institutional Biosafety Committee](#) as well as obtain IRB approval. Biohazardous materials include: recombinant DNA (e.g., plasmids or viral vectors); potentially infectious microorganisms (e.g., viruses, bacteria, fungi, prions, etc.); biologically derived toxins, such as those classified as Select Agents and human cell lines, tissue, blood, or other human/nonhuman primate materials.

RADIATION SAFETY COMMITTEE (RSC)

The [Radiation Safety Committee](#) evaluates all proposals involving [use of radioactive materials](#) and radiation-producing equipment within the University. All studies that use radiation exposure for investigational purposes that is not clinically indicated and/or that differs from standard clinical practice, requires Radiation Safety Committee (RSC) approval. This includes CT scan/PET scans, etc. that are being done for research purposes and that are not considered standard of care for the study.

RSC Contact Information:

Phone: (323) 442-2201

All new studies that use radiation in an investigational manner must receive approval by the RSC in addition to IRB approval prior to initiating the study. An RSC “Application for Use of Radiation Producing Devices in Clinical Research” is submitted to the RSC with a copy of the IRB application, the Informed Consent Form(s), and sponsor’s protocol (if applicable). The Radiation Safety Committee meets at least quarterly. RSC review produces an approval letter that must be uploaded onto iStar.

The **Radioactive Drug Research Committee (RDRC)** functions as a subcommittee of the USC Radiation Safety Committee, although it is sanctioned as an independent entity reporting to the FDA under the provisions of 12 CFR 36.1. It provides a vehicle to use radioactively labeled agents or drugs to be used in human imaging research for purpose of obtaining information about their basic pharmacology, biodistribution, and dosimetry (usually 30 or fewer patients per trial). These agents, or their parent molecules, are required to have already been used in human subjects, where toxicology is known, or they are a naturally found agent within the body such as an amino acid. The process allows this type of research without the need for an IND; an IND would be required to research larger patient populations, where there is no prior human use, or where the purpose is to study efficacy, as examples. All RDRC protocols must also be approved by the USC IRB and by the USC Radiation Safety Committee. The RDRC membership includes physicians, physicists, radiochemists, radiation safety and administrative staff, and any other ad hoc specialists that might be needed for the particular type of studies to be performed.

STEM CELL RESEARCH OVERSIGHT (SCRO) COMMITTEE

The [Stem Cell Research Oversight Committee](#) reviews, approves, and provides oversight over all issues related to the derivation and use of human pluripotent stem cells. Research under SCRO jurisdiction may not begin until approved by the SCRO.

SCRO Contact Information:

E-Mail: StemCell@med.usc.edu

CONFLICT OF INTEREST REVIEW COMMITTEE (CIRC)

The [Conflict of Interest Review Committee](#) (CIRC) is charged with reviewing disclosures of conflicts of interest related to research and formulating recommendations on how to manage conflicts in a manner that preserves the objectivity of research in instances where a conflict exists. CIRC also reviews external assessments performed in instances of institutional conflict. CIRC meets monthly and is comprised of faculty and administrators.

CIRC Contact Information:

Phone: (213) 740-2500

Remember that all potential conflicts must be disclosed through “[diSClose](#)”, USC’s on-line conflict disclosure system. (<https://disclose.usc.edu>). Also, all investigators supported by Health and Human Service (HHS) agencies (such as NIH, AHRQ and CDC) are required to submit an annual disclosure of all financial interests related to their institutional responsibilities at USC via diSClose. Annual disclosures must be updated between **June 1st and July 31st each year**. Additional updates may be required when changes occur during the year. Investigators are not permitted to submit proposals unless their disclosures are up to date.

CLINICAL INVESTIGATIONS COMMITTEE (CIC) — USC NORRIS COMPREHENSIVE CANCER CENTER (NCCC)

The Clinical Investigations Committee (CIC) is a multidisciplinary scientific peer review committee that is established to fulfill the National Cancer Institute requirement for a Protocol Review and Monitoring System at NCI designated comprehensive cancer centers. The CIC review is designed to ensure that clinical research trials at the USC Norris Comprehensive Cancer Center are of the highest scientific quality and integrity by review of the scientific merit, feasibility, priorities and progress. The committee is composed of 26 faculty members with representation from medical oncology, hematology, radiation oncology, radiology, surgery, neurologic oncology, gynecologic oncology, and preventive medicine. Furthermore, the committee has three senior statisticians and several managers from CISO who focus on operational aspects of clinical trials.

CIC Contact Information:

E-Mail: CoreCISO@med.usc.edu

All clinical and translational protocols at USC that involve human subjects and are designed to address a cancer focused scientific question must be reviewed and approved by CIC prior to IRB review and approval. The cancer-focused scientific question may be related to cancer diagnosis, screening, prevention, or treatment. It is relevant to note that CIC is not only an oversight committee, but also a critically important resource; the CIC members and reviewers are experienced trialists and scientists who can provide very important and constructive feedback that improves the study design and conduct, and therefore benefit the investigator’s research.

More information about the CIC can be found in the USC Norris Cancer Center [Clinical Investigator's Manual](#), developed by CISO.

QUALITY ASSURANCE MONITORING COMMITTEE (QAMC) — NORRIS COMPREHENSIVE CANCER CENTER (NCCC)

The [QAMC](#) has two main functions: 1) to monitor study accrual and progress at regular intervals; 2) to ensure quality in study conduct through the performance of audits on investigator initiated/institutional trials as well as NCI supported trials, the review of all protocol violations, and the review of protocol amendments. It is not infrequent for the QAMC to proposed amendments to the investigator in order to ensure that the study is performed with the highest degree of compliance as well as optimize the chances of being able to address the endpoint of the trial. The QAMC meets on a monthly basis. All clinical trials that have been approved by the CIC are subject to QAMC oversight.

QAMC Contact Information:

<http://oprs.usc.edu/2013/05/13/usc-cancer-center-coordinators-invited-to-serve-on-quality-assurance-committee/>

DATA AND SAFETY MONITORING COMMITTEE (DSMC) — NORRIS COMPREHENSIVE CANCER CENTER (NCCC)

The [Data and Safety Monitoring Committee](#) (DSMC) is an independent body responsible for the safety of study subjects through the review of new protocols to ensure an adequate adverse event assessment/reporting plan, study stopping rules and through the real-time and periodic monitoring of severe adverse events (SAEs) or those AEs that require expedited reporting. The DSMC performs quarterly and annual safety reviews as well as interim efficacy/futility analyses on institutional trials.

DSMB Contact Information:

E-Mail: CoreCISO@med.usc.edu

PHASE I COMMITTEE — NORRIS COMPREHENSIVE CANCER CENTER (NCCC)

All Phase I trials are reviewed by the Phase I Committee that meets twice a month. It is responsible for reviewing and adjudicating all dose-limiting toxicities (DLT), dose escalations and appropriateness of the escalation, cohort expansion, subject replacements and confirmation of attainment of maximal tolerated dose. Each patient is reviewed individually after the end of their DLT/assessment period and evaluability/replacement and DLT are determined, as specified in the protocol. All findings are documented in CAFÉ (see below). Special toxicities are queried as needed and a summary is

Phase I Committee Contact Information:

E-Mail: CoreCISO@med.usc.edu

prepared and made available to the CIC, QAMC and DSMC. The Phase I committee also maintains a waiting list of all patients waiting for slots and assigns slots to patients as they become available.

3. OTHER RESOURCES & ENTITIES

CANCER CENTER DATABASE (CAFÉ)

Cancer Center Database (CAFÉ): [CAFÉ](#) provides platform for creation of Research Database Applications. CAFÉ is an object-oriented development environment which empowers developers to create applications quickly and inexpensively. CAFÉ was initially developed for protocol management, patient enrollment and electronic data capture to manage clinical and translational research studies at the USC Norris Cancer Center. It has now been generalized and has been used for tissue microarray data capture, epidemiologic studies, prevention trials, laboratory management, tissue repositories and administrative systems at USC. For investigator initiated studies at the Norris Comprehensive Cancer Center, electronic case report forms (eCRFs) must be developed prior to opening a trial to enrollment.

CAFÉ Contact Information:

Phone: (323) 442-7710

CAFÉ Tracker provides step-by-step protocol status information in real time from time of receipt of protocol by CISO until the study is open to accrual. The Regulatory Manager assigned to the study is responsible for updating the CAFÉ Tracker. At the beginning of each month, the investigators receive an automated email from the Regulatory Manager generated by CAFÉ providing the status of their studies. Investigators also receive email reminders with deadlines for CIC protocol submission forms and CIC stipulation submission. These email reminders help investigators to track the progress of their studies. The reminder and status emails stop once the study is open to accrual.

RESEARCH FACILITIES & CORE LABORATORIES AT USC

USC's [research facilities and core laboratories](#) support the conduct of research and clinical trials through services in critical areas such as high performance computing, genomics, cellular and molecular analysis, biomedical imaging, nanoscience, and data analysis and management. Core laboratories offer shared-use research facilities and provide technological support for research projects carried out by faculty across academic disciplines and clinical specialties. Contact information for USC research facilities and core laboratories is provided in **Appendix 4**.

OFFICE OF RESEARCH ADMINISTRATION (KSOM)

The [Office of Research Administration](#) at the KSOM oversees grant and contract administration and research compliance to support and facilitate funding and adherence to university and federal, state and local regulations and sponsor policies and procedures. It serves as the point of contact for KSOM research faculty to obtain Dean's approval of grant or contract submissions, exceptions to F&A rates, advance funding, pre-award costs, cost sharing and transfer of unexpended fixed price contract balances. The office provides support to investigators in the following areas: (1) Grant submission and post-award; (2) Training (seminars & on-line, as needed) and (3) Compliance (in conjunction with the USC Office of Compliance).

USC OFFICE OF RESEARCH

The [Office of Research](#) supports individual and interdisciplinary research that addresses societal needs. The office invests in research initiatives, promotes USC research among sponsors, and provides services that ensure USC achieves the highest ethical standards in its research. Offices/units that fall under the Office of Research include: the [Research Advancement Office](#) (Washington, DC), the [Department of Contracts & Grants](#), the [USC Stevens Center](#) for Innovation, Institutional Review Boards ([Office for the Protection of Research Subjects](#)), the [Department of Animal Resources](#) and the [Institute for Creative Technologies](#). The office is the university point of contact for issues such as:

- Complaints pertaining to research misconduct.
- Identifying sources of research funding, both inside and outside the university.
- Support for submission of research proposals.
- Participation in, and initiation of, major inter-disciplinary university research programs and formation of research units.
- Education to prepare investigators for funding strategies and proposal preparation.
- Clearance for research competitions that limit the number of proposals submitted by the University.

Office of Research Contact Information:

Phone: (213) 740-6709
E-mail: Vprsch@usc.edu

DEPARTMENT OF CONTRACTS AND GRANTS (DCG)

The [Department of Contracts and Grants](#) supports USC's investigators through proposal submission, award negotiation, sub-awards, award set-up and award close-out, ensuring that grants and contracts are consistent with

DCG Contact Information:

HSC Phone: (323) 442-2396
UPC Phone: (213) 740-7762

university standards for academic freedom, research ethics and fiscal responsibility. While the DCG does not prepare proposals or budgets for basic research proposals, its clinical trials office provides this service for industry-sponsored trials.

USC STEVENS CENTER FOR INNOVATION (SCI)

The [USC Stevens Center for Innovation](#) is a university-wide resource for USC innovators. The Center manages the intellectual property portfolio and technology transfer process for the university, as well as provides ongoing review and updating of relevant university policies. It collaborates with all [17 schools and the College](#) at USC to promote existing programs and develop new ones by providing USC investigators with greater access to technology translation professionals, expanded startup support services and a streamlined industry interface. Support services also include identification of translational funding and mentoring opportunities.

SCI Contact Information:

Phone: (213) 821-5000

II. USC CLINICAL TRIALS OFFICE (CTO)

1. Introduction
2. Contract Review, Negotiation, and Execution
3. Coverage Analysis
4. Budget Development and Negotiation
5. From CDA to Clinical Trial Agreement and Study Activation
6. Roles of the Study Team

1. INTRODUCTION

USC has established a [Clinical Trials Office](#) (CTO) as a service center to support Principal Investigators and research sponsors in the creation of Clinical Trial Agreements (CTAs) that support development and testing of novel therapies, devices and diagnostics. The CTO's operations have three main components:

- Contract Review, Negotiation, and Execution
- Coverage Analysis
- Budget Development and Negotiation

The CTO works in concert with a co-located team from [Sponsored Projects Accounting](#), which invoices and collects payments for sponsors, as well as reviews and reimburses sponsor reimbursable clinical costs.

The CTO is divided into teams, each responsible for a number of departments. Each team comprises a Sr. Contract Manager, Budget Specialist and Coverage Analyst.

2. CONTRACT REVIEW, NEGOTIATION, AND EXECUTION

The CTA is the contract between the university and a sponsor and defines the work to be done on a clinical trial as well as the mutual obligations. For example, a CTA will state contract terms associated with:

- Amount that USC will be reimbursed for work on a trial, and the conditions by which USC will be paid (e.g., start-up costs and per-patient enrollment costs);
- Obligations to protect confidential information;
- Rights of the sponsor to monitor the work at USC, and to inspect patient records;
- Liability in case something goes wrong in a trial;
- Rights to intellectual property created prior to and during the trial;
- Rights of the university to publish research that relies on data collected during the trial;
- Study related Principal Investigator (PI) and USC obligations including reporting of Adverse Events and other reports prepared pursuant to the study protocol; and
- Study period and procedures associated with early termination of the study.

The CTO negotiates with the sponsor to ensure that the contract terms are reasonable and fair, while aiming to start trials and enroll patients as quickly as possible.

The Sr. Contract Manager is responsible for negotiating the non-financial terms of the CTA. The starting point for this work is typically a template agreement provided by USC or, more commonly, by the sponsor. In some cases, USC has negotiated a master agreement with a sponsor that pre-determines many of the terms and conditions, thus expediting negotiations.

When a template comes from the sponsor, the proposed CTA includes the industry sponsors' preferred contract terms. The Sr. Contract Manager is responsible for reviewing these CTAs in order to identify terms and conditions that are inconsistent with governing federal regulatory policies and regulations (e.g. FDA, HIPAA privacy rules) and USC policies and regulations with respect to subjects, such as dissemination of research results and management of potential intellectual properties developed during the performance of the study, in accordance with sponsor's protocol. The Sr. Contract Manager will focus on finding compromise language that is acceptable to both USC and the industry sponsor. During this process, the Sr. Contract Manager may consult with and receive input from the Principal Investigator, USC Office of the General Counsel, USC Stevens Center for Innovation, and USC Department of Risk Management and Insurance, as needed. Upon finding mutually acceptable alternatives for all disputed terms (except the budget and payment schedule), the Sr. Contract Manager will facilitate the development of a clean copy of the negotiated CTA that is ready for signatures pending the completion of negotiations conducted by the Budget Specialist (i.e. the CTA budget and payment terms).

As explained later, the CTO's practice is to negotiate budget and payment terms in parallel with other types of contract terms. In some cases, depending on the items in dispute, this means the budget and payment negotiations may have been completed before or after the completion of the Sr. Contract Manager's work. In such instances, the clean copy of the negotiated CTA will be ready for signatures.

3. COVERAGE ANALYSIS

While the Sr. Contract Manager is beginning his or her work on reviewing the CTA, the Clinical Trial Financial Administrator will simultaneously begin working on developing a study-specific Coverage Analysis that identifies and distinguishes any and all costs that must be charged to the sponsor (research-related) from those routine patient care costs that could be charged to private insurance or Medicare, as applicable. The Financial Administrator will use the sponsor's protocol (it could be industry sponsor or a study sponsored by the Principal Investigator) and resources, such as the Medicare National Coverage Determination Manual:

(<http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals->

[IOMs-Items/CMS014961.html](#)) and [Current Procedural Terminology](#) (CPT®) codes to determine those costs that are considered routine patient care. Once the coverage analysis is completed, it is sent to the Budget Specialist and the Principal Investigator. The coverage analysis provides the distinctions and identifications that are used in the process of developing a clinical trial budget that is consistent with the federal government and USC requirements.

4. BUDGET DEVELOPMENT AND NEGOTIATION

The Budget Specialist starts to build USC's first response to the sponsor's proposed budget after receiving the completed coverage analysis. The Budget Specialist works with Principal Investigators, Study Coordinators, department financial administrators, and representatives from other participating units to produce a comprehensive budget that will facilitate the process of negotiating the budget and payment terms with the sponsor. In addition to completed coverage analyses, the Budget Specialist utilizes the study protocol, sponsor's budget spreadsheet, informed consent, and contract payment terms to complete the development of USC's first budget. USC's first budget is then sent to the sponsor for their review and response. This is where the budget negotiations will begin in order to focus on differences between USC and the sponsor's budgets. Upon reaching an agreement with respect to the budget and the payment schedule, the Budget Specialist is charged with finalizing the entire Clinical Trial contracting process (assuming that the contract term negotiations are completed as well). This process includes collection of all the necessary documents (including a fully executed CTA with the final budget and payment schedule) and performance of all the required data entries and verifications in Database Management System (DBSMs) such as iStar, TRUE, TRUE2, and IRIS. As a part of this process, the signed CTA and other relevant documents are sent for [Kuali Coeus](#) (KC) entry, which in turn will start the post-award management of the clinical trial through activities such as creation of a financial account, initiation of invoicing/billing, and the conduct of necessary monitoring procedures.

For PI-initiated clinical trials, the Budget Specialist will work with the Principal Investigator to develop a preliminary budget that could be considered by the funding collaborator of the study.

5. FROM CONFIDENTIALITY AGREEMENT (CDA) TO CLINICAL TRIAL AGREEMENT AND STUDY ACTIVATION

In many instances, the process of collaboration with industry sponsors begins with the review of their confidential/proprietary information related to a study protocol, drug or a device, or a procedure by an interested USC faculty member. This exchange of information is facilitated through a Confidentiality Agreement. As of this point, this faculty member is identified as the Principal Investigator (PI) representing USC in reviewing the sponsor's confidential information

and making a decision about participating in a sponsored-initiated clinical trial. In a PI-initiated clinical trial, USC faculty member is the initiator of the study plan/ protocol.

6. ROLES OF STUDY TEAM

The following bullet point steps illustrate the process lifecycle for CTO's most frequent activities, identifying the specific responsibilities of the study team:

Confidentiality Agreement

- Initiate a CDA submission by submitting through TRUE2.
- After negotiation of CDA language, the PI should sign to indicate that he or she reads and understands the language (prior to signature by the CTO's contract negotiator).
- Once CDA is executed, insure that information is kept confidential and only provided to people at USC on a "need to know" basis. Those who need to receive information should be given access to the minimum amount of confidential information necessary to effectuate the study, informed of its confidentiality, and informed that confidential information should never be shared outside of USC.

Clinical Trial Agreement (Sponsored-initiated)

- Initiate a clinical trial submission through TRUE2.
- Include the study protocol authored by sponsor, sponsor's proposed Clinical Trial Agreement (CTA), lab manual(s) and sponsor's proposed budget in this submission.
- Respond to queries from budget specialist regarding budget parameters as first response to sponsor's initial budget.
- Approve budget once negotiated, including the final signature and approval by Department Chair or designee of Department Chair.
- Submit protocols for all relevant regulatory approvals, including IRB and conflict of interest (if applicable).
- Once study is activated by CTO's budget specialist in TRUE, execute clinical trial in accordance with approved protocol and CTA.

Clinical Trial Agreement (PI- initiated)

- Initiate a clinical trial submission through TRUE2.
- Include the study protocol authored by the Principal Investigator, sponsor's proposed Clinical Trial Agreement (CTA), if available, and Principal Investigator's proposed budget.
- Respond to queries from budget specialist regarding budget parameters as required to cover the study costs.
- Approve budget once negotiated or as applicable when consistent with funding

sponsors cap or limitations including the final signature and approval by Department Chair or designee of Department Chair.

- Submit protocols for all relevant regulatory approvals, including IRB and conflict of interest (if applicable).
- Once study is activated by CTO's budget specialist in TRUE, execute clinical trial in accordance with approved protocol and CTA.

Coverage Analysis for Non-industry Sponsors

- Initiate coverage analysis request in TRUE2
- PI should review and approve coverage analysis determination showing activities that will be paid by sponsor, insurer or other USC account.
- Once study is activated by CTO's budget specialist in TRUE, conduct clinical trial in accordance with approved protocol and CTA.

Execution of Clinical Trial:

REGISTERING PATIENTS, RESEARCH ORDER FORMS AND APPROVAL OF EXPENDITURES

GE Centricity Business/GECB/ Billing System

- SPA/Clinical Trials Office will register participants study information and financial class in GECB Billing System within 24 hours of notification of enrollment from study team. This will activate the Clinical Trials Patient Alert (Flag) to Keck, Norris and USC Care providers. An email notice will be sent announcing the enrollment of a new participant to a study.

TRUE: Trial Registration Update Entry

- This is a database maintained by SPA/Clinical Trials that contains study participant information, study calendar, research order form and coverage analysis for clinical trials.

For studies that are ongoing and actively enrolling participants

- SPA/Clinical Trials Office will update the website with the current participant Consent and HIPAA forms, study dates on and off once it is provided to us. Forms should be faxed to 323-865-7791/323-865-9234 within 24 hours after consenting a participant to a study.

Research Order Forms (ROF)

- When a research participant is scheduled for study related tests and procedures, these items should be ordered using the Research Order Form. This is a study specific order form that defines which services are provided as part of a research study on a particular

date of service. Billing Auditors will use the completed and signed ROF to bill charges to the appropriate payer based upon the coverage analysis.

III. COMPLIANCE

1. Considerations Related to Clinical Trials
2. HIPAA Privacy Rule
 - Roles and Responsibilities of Research Coordinators
3. Clinical Trials Billing
 - Roles and Responsibilities of Research Coordinators
4. Conflict of Interest Related to Research
 - Roles and Responsibilities of Research Coordinators
5. Confidentiality Agreements and Clauses
 - Roles and Responsibilities of Research Coordinators

1. CONSIDERATIONS RELATED TO CLINICAL TRIALS

USC's [Office of Compliance \(OOC\)](#) 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;
- Investigates allegations of non-compliance and recommends corrective action where appropriate.

As relevant to research coordinators, the OOC provides guidance on issues related to Privacy and Security, Conflicts of Interest, and Research Misconduct.

OOC Contact Information:

Phone:	213.740.8258
E-mail:	complan@usc.edu

The OOC 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.

Please visit <http://ooc.usc.edu> for additional information.

2. 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.

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>.

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 practicably be conducted without the waiver or alteration;
- The research could not practicably 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>) 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.

USC's HIPAA Privacy and Security policies and procedures are available on the USC policies website at <http://policies.usc.edu/p2admOpBus/hipaa.html> or the USC Office of Compliance website at <http://ooc.usc.edu>.

ROLES AND RESPONSIBILITIES OF RESEARCH COORDINATORS

Working under the direction of the principal investigator, research coordinators:

- 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.

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.

3. 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 Coverage Analysis to determine which activities to be undertaken in connection with a clinical trial may appropriately be 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 coverage 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 tests and procedures identified in the study protocol. The ROF indicates which services should be billed to insurance or Medicare as applicable 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.
- 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.

4. 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.

5. 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.

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.

IV. PROTECTING HUMAN RESEARCH SUBJECTS AT USC

1. Human Subjects Research Overview
 - Human Subjects Research/Clinical Trial Defined
2. Regulatory Authorities
 - Office for Human Research Protections (OHRP)
 - Food and Drug Administration (FDA)
 - Health Insurance Portability and Accountability Act (HIPAA)
 - California State Laws
 - USC Institutional Policies and Procedures
3. Review and Approval of Research
 - IRB Defined
 - iStar IRB Application System
 - Education Requirements for Study Staff
 - Training and Job Classification
 - Informed Consent
 - Certificates of Confidentiality (COC)
 - Departmental Review
 - Ancillary Committees and other Entities
 - Data Safety Monitoring Boards
 - ClinicalTrials.gov
 - Levels of IRB Review
 - Continuing Review
 - Amendments
 - Reportable Events
 - Significant New Information/Findings (SNIF)
 - Study Close Out
4. Summary of the IRB Submission Process for Clinical Trials at USC
5. References

1. HUMAN SUBJECTS RESEARCH OVERVIEW

The University of Southern California is committed to conducting its biomedical and behavioral research involving human subjects under rigorous ethical conditions. All human subjects research at USC must receive IRB review. The University's Institutional Review Boards (IRB) comply with federal, state, and local regulations.

The University has also agreed to adhere to the statements of ethical principles as described in [The Nuremberg Code](#), [The Belmont Report: Ethical Principles and Guidelines for the Human Subjects of Research](#), and the [Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research](#).

This fundamental commitment to the protection of human participants applies to all USC research involving human participants regardless of whether the research is funded through the university, the federal government, a non-profit or industry sponsor and regardless of the location of the research.

Among the goals of the USC Human Subjects Protection Program (HSPP) are to assure excellence of the HSPP, maintain innovative and compliant [Human Subjects Policies and Procedures](#), and retain accreditation. A university-wide research ethics program and continuing educational programs assure that USC remains ahead of ever changing ethical and regulatory standards.

This chapter will describe the role of regulatory bodies, the IRB application process, and the role of RCs and investigators in human subjects research at USC including informed decision making, protecting subjects, and enabling research to proceed.

Overall, the PI is responsible for the entire study and the research coordinator is responsible for implementing the study and supporting the ethical, regulatory, and sponsor requirements.

HUMAN SUBJECTS RESEARCH/CLINICAL TRIALS DEFINED

At USC, studies that use human participants to evaluate or understand drugs, devices, biologics and answer questions of a social-behavioral nature are subject to federal, state, local laws and institutional policies. Human subjects research involving an unapproved FDA regulated test articles and one or more human subjects and/or the results are intended to be submitted later to the FDA as part of an application for a research or marketing permit is a clinical trial. For purposes of this chapter, "clinical trials" and "clinical investigations" are synonymous with human subjects research.

The federal definitions of both "research" and "human subjects" must be met for a study to be

classified as “human subject research”.

Research – “a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge” (45 CFR 46).

Human Subject – “a living individual about whom an investigator (whether professional or student) conducting research obtains: data through intervention or interaction with the individual, or identifiable private information”. In **FDA regulated research**: a human subject is “an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.”

2. REGULATORY AUTHORITIES

National, local, and institutional entities establish the laws and regulations by which human subjects research must be conducted. RCs and PI should have a familiarity with the general functions and missions of these organizations. An overview follows. The laws and policies governing the conduct of human subjects research can be complicated. If you are not certain what your obligations are in a given situation, contact [Office for the Protection of Research Subjects](#) (OPRS) or the [Office of Compliance](#).

OFFICE FOR HUMAN RESEARCH PROTECTIONS (OHRP)

The Office for Human Research Protections (OHRP/HHS), is charged with ensuring that institutions receiving federal funding protect the rights, welfare, and well-being of subjects involved in research. In order to receive research support from HHS, Department of Defense, Department of Energy, or other federal sponsors of human subjects research, an institution must execute a Federalwide Assurance (FWA) where it represents that it will comply with the Common Rule ([45 CFR 46](#)). Each department or agency that provides research funding may have requirements beyond what is described in the Common Rule.

In addition, OHRP provides educational programs and materials, maintains regulatory oversight, and offers advice on ethical and regulatory issues related to human subjects research. OHRP provides guidance documents on topics such as informed consent, vulnerable populations, and protocol review. These documents are all available on the OHRP website www.hhs.gov/ohrp

OHRP conducts not-for-cause audits of institutions/investor, and receives, reviews, and responds to incident reports from “assured” institutions. OHRP audits usually result in a “Determination Letter” issued to the institution /investigator associated with the research that it inspects. These Determination Letters are made public on the OHRP website and represent

the office's position on compliance issues.

An RC or Principal Investigator (PI) may contact OHRP directly for inquiries related to your studies.

FOOD AND DRUG ADMINISTRATION (FDA)

The U.S. [Food and Drug Administration](#) (FDA / HHS), regulates clinical research on drugs, devices, and biologics. The FDA is responsible for assuring the safety, efficacy, and security of these experimental therapies or diagnostics.

The FDA is also responsible for reviewing clinical trial applications for investigational drugs and devices and biologics. These are known as IND (Investigational New Drug), IDE (Investigational Device Exemption), and biologic license applications.

RCs and PIs should be familiar with the sections of [Title 21](#) of the FDA Code of Federal Regulations that pertain to drugs, devices, biologics and financial disclosure. The FDA also publishes guidance and updates each year on topics such as drug safety, pharmacology, IRB responsibilities, and monitoring practices, in addition to others. You may read or download these documents from the [FDA website](#). Determination letters detailing findings that the FDA has identified for correction in clinical trials it regulates are found here: www.fda.gov

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA)

The Health Insurance Portability and Accountability Act (HIPAA), also known as the “Privacy Rule”, establishes minimum Federal standards for safeguarding the privacy of individual's identifiable health information. The law, overseen by the Office of Civil Rights within HHS, generally prohibits health care providers such as health care practitioners, hospitals, nursing facilities and clinics from using or disclosing protected health information (“PHI”) without written authorization from the individual.

USC requires all faculty, staff and other USC employees, as well as students, volunteers, agents and certain other individuals who have access to patient health information through USC providers, to complete an online course on the HIPAA Privacy Rule. The course may be accessed on the Office of Compliance website:

<http://ooc.usc.edu/hipaa-privacy-education-program>

CALIFORNIA STATE LAWS

In addition to federal regulations, researchers are also expected to follow California laws addressing human subjects research. The California Health and Safety Code contains provisions addressing human subjects research (HSC 24170). If you have questions regarding how to apply state regulations to a specific research project, you should contact the Chair of the IRB ([UPC](#) or [HSC](#)) and/or the [Office of Compliance](#).

USC INSTITUTIONAL POLICIES AND PROCEDURES

The USC [Human Subjects Protection Program](#) (HSPP's) addresses the regulation, approval, and oversight of human subjects involved in research conducted under the auspices of the University. USC's Policies and Procedures for Human Subjects Research are periodically revised to remain current with federal and state regulations as well as institutional policies and Good Clinical Practices (GCP). Research Coordinators and other study staff are encouraged to regularly consult the policies and procedures during the submission, review, and conduct of human subjects research.

These policies and procedures address most research situations involving human subjects. If an issue arises that is not addressed by the policies, or you do not know how to apply policies, contact the IRB.

<http://oprs.usc.edu/rules/>

3. REVIEW AND APPROVAL OF RESEARCH

Institutional Review Boards are committees charged with reviewing research activities involving human subjects that are conducted at an institution or by an institution's faculty and students. The federal government and many organizations that fund research require IRB review of the research they fund. Unfunded or investigator-initiated research also requires IRB review.

IRB DEFINED

USC's Institutional Review Board (IRB) is charged with assuring that the rights, safety, and well-being of human subject participants is maintained and that research is conducted in a manner consistent with the approved protocol. The IRB reviews research protocols to ensure the activity complies with University policies as well as federal, state, and local laws. The IRB has the authority to approve, require changes to the study procedures, or disapprove proposed research projects.

At USC, there are four IRBs: one on the University Park Campus that primarily reviews social/behavioral research and three on the Health Sciences Campus that primarily review biomedical research. Researchers may be required to get approval from additional bodies before the IRB will conduct a review. These are called ancillary committees. Examples include institutional biosafety and radiation safety (see **Chapter VI** for more details on ancillary Committees).

Federal regulations require that the IRB have at least five members. These members must include individuals from academic disciplines relevant to the research being reviewed and must include at least one non-affiliated member (at USC this person is referred to as a Community Member). The IRB should be diverse in terms of race, gender and cultural background. IRB members can be faculty, staff or students from the institution, as well as members of the local community. IRB members must have the necessary experience and expertise to competently evaluate the proposed research.

In the review process, the IRB may approve, defer, or approve with contingencies. Contingencies are modifications required by the IRB.

The IRB reviews the following aspects of each study:

- Description and research methodology*
- Equitable selection of subjects*
- Risks minimized*
- Acceptable ratio of risks to benefits*
- Vulnerable status of subjects*
- Incentives for participation
- Privacy and confidentiality*
- Monitoring (frequency and mode)*
- Informed consent content (required elements and types) and process*
- Conflict of interest
- Departmental resources/appropriate expertise of PI and study staff
- Sponsor Requirements
- Scientific values
- HIPAA requirements

** Approval criteria for IRB review of research*

ISTAR IRB APPLICATION SYSTEM

The IRB Submission Tracking and Review System (iStar) is the online IRB application system

used at USC. All IRB related correspondence and documentation must be submitted online through iStar. An iStar training site, FAQ's, how to create an iStar account and other information may be found at oprs.usc.edu/istar

iStar is used for the following functions, among others:

- Create and edit an electronic application for submission to the IRB
- Identify study staff
- Attach study documents
- Track the progress of an application as it is automatically routed for review and signoff to the appropriate organizations (i.e., division and department reviewers) before being received by the IRB
- Communications between IRB and study staff
- Receipt and download of approval letter and all approved study documents

The RC is often responsible for the iStar submission. The PI, however, must always review and approve it before it is submitted for IRB review. The PI must personally answer conflicts of interest questions though the RC may verify that this is completed. Changes to the IRB submission required by the sponsor as well as other sponsor interactions are the responsibility of either the RC or PI.

EDUCATION REQUIREMENTS FOR STUDY STAFF

The IRB requires that the RC, PI and all other study personnel complete training on conducting human subjects research. These requirements vary according to the type of research, funding, and roles of the individuals involved in research. All training required by the USC IRB is available online through CITI.

<http://www.citiprogram.org>

COURSE	REQUIREMENTS	DESCRIPTION
Human Subjects Protections	Mandatory for Principal Investigators and Key Personnel conducting human subject research. “Refresher” training must be repeated every 3 years.	Pertains to ethics and principles, laws and regulations, informed consent, vulnerable populations, and more.

Good Clinical Practice (GCP)	Mandatory for Principal Investigators and Key Personnel conducting Full Board clinical trials research. GCP training is only required once.	Pertains to data credibility and accuracy, protection of subject rights, safety, and confidentiality of subjects/data.
Responsible Conduct of Research (RCR)	Mandatory for all students on NSF grants, as well as some NIH training awards, and PHS traineeships. Cannot be substituted for Human Subjects Protections training.	Pertains to ethics, data integrity, collaborative research, and more. The USC Office of Compliance provides the certificate of completion.
Conflict of Interest	Mandatory for all HHS investigators. Must be retaken every four years.	Pertains to the responsibilities of investigators and institution in managing conflicts of interest
Health Insurance Portability and Accountability Act (HIPAA)	Mandatory for Principal Investigators and Key Personnel who have access to private identifiable health information.	Pertains to Federal Privacy Rules (available on USC Office of Compliance).
Grants Management Training	Mandatory for all parties requesting expenditure /approval authority on accounts.	Pertains to fiscal and administrative responsibilities of sponsored research.

TRAINING AND JOB CLASSIFICATIONS

Staff and faculty engaged in clinical research are expected to have training and experience appropriate to their positions. Clinical research staff may fall in one of these positions, depending on their job responsibilities:

RN RCs

Research Nurse: Functions as a team member in the recruitment, assessment, treatment, data collection and follow-up for patients enrolled in a research study.

Research Nurse Senior: Functions as a team member in the recruitment, assessment, treatment, data collection and follow-up for patients enrolled in a research study.

Protocol Coordinator: Assists principal investigator in coordinating all phases of research studies including recruitment, assessment, treatment, data collection and follow-up for enrolled patients. Provides input to principal investigators, staff nurses and patients that effects clinical research studies from the initial protocol design to completion of study.

Sr. Protocol Coordinator: Serves as a team leader in the recruitment, assessment, treatment, data collection and follow-up for patients enrolled in a research study. Provides leadership and direction for daily research study operations and administrative activities. Assists principal investigator in coordinating all phases of research studies. Provides input to principal investigators, staff nurses and patients that effects clinical research studies from the initial protocol design to completion of study and final publication.

Non-RN RCs

Research Coordinator I: Assists investigators or other staff with research studies in subject recruitment, data collection, scheduling of study-related activities and follow-up of enrolled subjects.-

Research Coordinator II: Serves as a lead coordinating aspects of sponsor-initiated and investigator-initiated research studies including subject recruitment, data collection, scheduling of study-related activities and follow-up of enrolled subjects. Assists with budget preparation and training of less experienced research coordinators. Provides guidance and direction related to research studies to investigators, research personnel, and subjects, from initial protocol design to completion of study and close-out report.

Research Coordinator Supervisor: Supervises and coordinates all aspects of sponsor-initiated and investigator-initiated research studies including subject recruitment, data collection, scheduling of study-related assessments and follow-up of enrolled subjects, budget development and administration. Supervises staff and plans project operations

based on proposed research activities and timelines. Provides leadership, guidance and direction related to research studies to investigators, research personnel and subjects, from initial protocol design to completion of study and close-out report.

Clinical Research Data Specialist: Lead Coordinates, facilitates and manages the clinical data for various phases of complex clinical trials. Assists Study Coordinators and Clinical Research Data Specialist II with complex clinical trials. Provides leadership, guidance and direction to Clinical Research Data Specialists.

Clinical research staff who are not classified in one of these positions should contact their department to request a review of their position and appropriate reclassification.

All clinical research and staff are strongly encouraged to complete the Orientation to Clinical Research at USC course, available online at: <https://research.usc.edu/orientation-to-clinical-research-at-usc/>. In addition, all employees classified as Research Coordinator II or Research Coordinator Supervisor are required to obtain clinical research certification, such as the certification offered by the [Society of Clinical Research Associates](#) (SOCRA). Other clinical research staff are strongly encouraged, but not required, to obtain certification.

Human subjects training, including [Good Clinical Practice](#), is offered by the Office for the Protection of Research Subjects. The IRB is responsible for ensuring that all appropriate human subject training has been completed for study staff.

Health Insurance Portability and Accountability Act (HIPAA) training is offered by the Office of Compliance. The IRB is responsible for ensuring that HIPAA training has been completed when required.

Staff and faculty may be required to complete additional training based on their job responsibilities. For further information, consult the [USC Research Training Finder](#). This site also provides information on USC's [Center for Excellence in Research](#), which offers a wide array of courses on research topics.

Staff may also consider enrolling in for-credit courses at USC for additional training. For instance, the [Regulatory Science Program](#) in the Department of Pharmacy offers courses on regulation of medical products, clinical trials, and drug development.

INFORMED CONSENT

RCs may be responsible for writing or administering [informed consent](#) and therefore need to be knowledgeable about both content and process. Informed consent is about protection and respect for research subjects. The requirement and content of consent varies according to the level of review and nature of the research. Informed Consent must contain:

- The purpose and procedures involved in the research
- Alternatives to participation All foreseeable risks and discomforts to the subject (e.g. physical injury, psychological, social, or economic damage)
- The benefits of the research to subject and/or society
- Person to contact for answers to questions or in the event of a research-related injury or emergency
- In the state of California, clinical trial subjects must be presented with a copy of the Experimental Subject's Bill of Rights

The USC IRB Informed Consent template can be found online at: <http://irb.usc.edu/hsirb-forms>.

Waiving one or more of the elements of informed consent may be permitted by the IRB for some research activities when justified. Informed consent elements that do not apply to a specific study need not be provided in the consent.

In all cases, the informed consent must:

- Be presented in a language understandable to the subject
- Minimize the possibility of coercion or undue influence
- Allow subjects sufficient time to consider participation
- Allow subjects to refuse or discontinue participation at any time
- Distinguish between research and routine medical care
- Be appropriately presented for the subject's physical, emotional and psychological capacity, and vulnerable status
- Assure that subject understands what participation entails

Other types of informed consent include: parental permission, assent, verbal consent, short form, and information/fact sheet. The study protocol and study population will dictate which of these are required. For further information on each, see the [OPRS website](#).

CERTIFICATES OF CONFIDENTIALITY (COC)

Certificates of Confidentiality are documents issued by the National Institutes of Health (NIH) and other federal agencies to protect identifiable research information from compelled disclosure. Certificates of Confidentiality are designed to protect subject data that, if disclosed, could have adverse consequences for subjects' financial standing, employability, insurability, or reputation. A Certificate of Confidentiality allows the researcher and others who have access to research records to resist providing subject information in any civil, criminal, administrative, legislative, or other proceeding at the federal, state, or local level. NIH funding is not necessary to obtain a Certificate of Confidentiality.

DEPARTMENTAL REVIEW

At USC, all research conducted on the Health Sciences Campus must have departmental approval before the IRB will conduct its review. The department chair must attest to the scientific merit and feasibility of the application, the availability of needed resources, and departmental acceptance of the study. This process also serves to alert department chairs of all research under their purview, as well as provide an opportunity to note potential conflicts of interest which they may be aware of due to their role of reviewing all outside consulting under the [Relationships with Industry policy](#).

ANCILLARY COMMITTEES AND OTHER ENTITIES

Depending on the nature of the study being proposed, approval from certain ancillary committees may be required before the IRB will issue final approval.

At USC, authorizations or approvals for research may be required from:

- [Clinical Investigations Committee \(CIC\)](#)
- [Clinical Trials Office \(CTO\)](#)
- [USC/LAC Departments of Pathology](#)
- [Stem Cell Research Oversight Committee \(SCRO\)](#)
- [Institutional Biosafety Committee](#)
- [Radiation Safety Committee](#)
- [Scientific Conduct Committee](#)
- Data Safety Monitoring Board/Committee
- [Conflict of Interest Review Committee \(CIRC\)](#)

While certain approvals must be obtained before IRB will issue final approval, others such as

CTO and pathology provide information or specimens and may be concurrent. The IRB will provide guidance to study staff questions regarding what ancillary approvals must be obtained based on materials, methods, or protocol. The CIC reviews all cancer studies before submission to the IRB.

DATA SAFETY MONITORING BOARDS (DSMB)

The purpose of a Data Safety Monitoring Boards (DSMB) is to independently evaluate data, ensure evaluate adverse event reporting, and suspend or terminate research when necessary. This oversight is distinct from areas the IRB reviews and approves. DSMBs may be required for clinical trials that are blinded, involve high risk intervention(s), and/or include vulnerable populations. There may be other cases where the IRB decides that DSMB oversight is necessary. The Clinical Investigations Support Office (CISO) has an ongoing Data Safety Monitoring Committee that regularly evaluates all cancer studies. All studies submitted to HSIRB must include a monitoring plan even when a DSMB is not required.

CLINICAL TRIALS.GOV

[ClinicalTrials.gov](https://clinicaltrials.gov) is a federal database for all publicly and privately supported clinical studies of human subjects conducted around the world. [The FDA Amendment Act \(FDAAA\)](#) of 2007 requires responsible parties in applicable clinical trials to register trials and submit summary results to ClinicalTrials.gov.

In addition to the FDA, some funding agencies may require registration. The site is a resource to patients who are seeking to participate in clinical trials, and helps ensure that null studies (studies with negative results) are published. Study subjects must be informed in the consent document that clinical trial information will be submitted to the National Institutes of Health/ National Library of Medicine (NIH/NLM) for inclusion in the clinical trial registry databank.

It is the sponsor's responsibility to register clinical trials when they begin, provide timely updates, and submit summary results to clinicaltrials.gov. Sponsor-investigator trials must be registered by the Principal Investigator. "Applicable Clinical Trials" include:

- **Drugs and biologics trials**— clinical investigations, other than phase I clinical investigations, of drugs or biological products subject to FDA regulation
- **Device trials** – trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and [pediatric postmarket surveillance](#) required by FDA <http://clinicaltrials.gov/>

LEVELS OF IRB REVIEW

The population being studied or the level of risk associated with a research activity will influence the level of IRB review. There are three levels of review:

- **Full Board Review**
 - Presents more than minimal risks to subjects and/or
 - Does not qualify for Expedited or Exempt Review

Examples of human subjects research activities reviewed by a Full Board convened IRB include novel investigations with experimental drugs or devices and documentation of illegal behaviors with links to subjects' identifiable information.

- **Expedited Review**
 - Meets one of the [9 federally defined Expedited Review Categories](#) (45 CFR 46.110)
 - Reviewed by an IRB Chair/designee/staff
 - Not greater than minimal risk (including privacy risk)

Examples of expeditable research activities include collection of blood samples from healthy adults, and collection of biological specimens or data by noninvasive means (saliva, cheek swab, x-rays).

- **Exempt Review**
 - Must meet one of the [6 federally defined Exemption Categories](#) (45 CFR 46.101)
 - Must be reviewed by an IRB Chair/designee/staff
 - Must not present greater than minimal risk* (including privacy risk)

* Minimal risk means 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.

Examples of Exempt research activities include measuring blood pressure and conducting anonymous educational tests.

CONTINUING REVIEW

In accordance with federal regulations, the USC IRB requires that ongoing research protocols undergo continuing review at intervals appropriate to the degree of risk, but not less than once per year. The frequency and extent of continuing review for each study is based upon study

type, risk, uniqueness of procedures, and vulnerability of subjects.

The continuing review application (in iStar) involves updates on the items requested in the initial submission, including any adverse events and any changes in number of subjects. Continuing review affirms that the study continues to sufficiently protect subject safety and welfare and that documentation of the study is complete, accurate, and up-to-date.

AMENDMENTS

Amendments are changes to an IRB-approved research protocol. Amendments must be submitted in iStar and approved by the IRB before being implemented. Examples include revisions to consent documents, changes in PI, and inclusion of additional risks. Amendments involving more than minor changes or changes that pose more than minimal risk will be subject to Full Board Review.

REPORTABLE EVENTS

Federally funded and/or FDA-regulated research must disclose the following to the sponsor, IRB, and (when requested) FDA or OHRP:

- Adverse Events
- Unanticipated problems involving risks to subjects or others
- Protocol violations
- Serious or continuing noncompliance with federal regulations
- Serious or continuing noncompliance with requirements of the IRB
- Suspensions or terminations of IRB approval

Reportable events must be disclosed to the IRB through the Reportable Events Application in the iStar system. Report contents must include the IRB study number; a detailed description of the event, incident, experience, and or outcome; and a description of corrective actions that have been taken or are proposed. The IRB determines when these events must be reported to federal agencies.

The different terms used by OHRP (Unanticipated Problems involving risks to subjects or others) and FDA (Adverse Events) are among the most common reportable events and easily confused. The table below distinguishes the two.

Regulatory Terminology for Unanticipated Problems vs. Adverse Events

	OHRP Protection of Human Subjects (45 CFR 46)	FDA Investigational New Drug Applications (21 CFR 312.32) Investigational New Device Exemptions (21 CFR 812.150)
Event Type	Unanticipated Problems Involving Risks to Subjects or Others	Adverse Events (Internal/External)
Context	Occurs in clinical or non-clinical research	Occurs in clinical research only
Scope	Untoward event in ANY aspect of a research study	Untoward response to a test article (e.g. drug, device, biologic)
Involve	Could be subject, study staff or others	Subjects only
Expectation	Unanticipated	<ul style="list-style-type: none"> Anticipated (an increase in frequency, duration or intensity beyond expectations) Unanticipated
Reporting	Prompt reporting to IRB required (not to exceed 10 working days)	Prompt reporting to IRB required (not to exceed 10 working days)
How to Report	iStar reportable event application	iStar reportable event application

SIGNIFICANT NEW INFORMATION/FINDINGS (SNIF)

Federal regulations require that subjects be provided with any significant new information or findings (SNIF) obtained during the course of the research that may affect a subject's willingness to continue participation.

A SNIF may be reported to the IRB by a study sponsor, PI or study staff. The IRB may require that all previously-enrolled subjects be provided with the new information one of two forms: (1) a summary of changes subjects need to know to remain in the study ([SNIF form](#)), (2) a revised [consent form](#). The IRB must review and approve the new information to be provided to the research subject prior to implementing changes that would result from the SNIF. When study changes are necessary to eliminate apparent immediate hazards to subjects, they may be

implemented prior to IRB approval but must be reported to the IRB. Keep in mind that the consent may have to be rewritten for all new subjects and re-consent may be required for currently enrolled subjects.

When appropriate, the SNIF form must clearly state that the information in the previously signed consent form remains current and valid. When the new information addresses several elements of informed consent and/or changes not easily described, the information should be incorporated into a revised consent document to provide sufficient context regarding new information and document the participant's decision to remain in the study.

Examples of situations that may require you to provide new information to subjects are as follows:

- Changes to the procedures that may affect a subject's willingness to continue in the research
- Identification of new risks or that risks previously described are known to occur with greater frequency or severity than previously reported
- Significant changes in costs to subjects
- New conflict of interest for a researcher
- Notification of findings from this study or related studies

STUDY CLOSE OUT

Upon study completion, the PI or other study personnel must submit a Close Study application to the IRB through the iStar system indicating the study status as "closed". Doing so confirms the study is finished and that no further interactions with subjects or their data will take place. A research project must be closed when subject accrual, subject follow-up and data analysis are completed. The IRB, in consultation with the RC or PI, may also close a study when active data analysis and publication have ceased, even if the researcher retains records that may identify individual subjects. Once a study is closed, no further research activity, including data analysis, may occur. Once the study is closed in iStar, yearly continuing review applications are no longer required. Additional research activities using data collected in an approved study may constitute new human subjects research studies subject to separate IRB review.

If a PI wishes to enroll new subjects to a closed study, a request can be made in iStar to reactivate the study. Once the study has been reactivated, a continuing review application must be approved by the IRB before study activities can resume.

It is permissible for a study to be closed at USC, and still be open to accrual at other sites. In the event that a serious adverse event or an unanticipated problem occurs at a non-USC site

after closure of the study at USC that may affect the study subjects, the USC RC is required to submit a report to the IRB via iStar.

4. SUMMARY OF THE IRB SUBMISSION PROCESS FOR CLINICAL TRIALS AT USC

Once the negotiations between the Clinical Trials Office (CTO) and the sponsor have taken place and the contract is established, the IRB submission may proceed:

- RC/PI obtain iStar account
- Takes required training
- Completes and submits IRB application (including Informed Consent)
- Obtains departmental review/approval
- IRB/Ancillary Committees review/approve application
- PI/RC address contingencies
- IRB accepts contingencies and issues approval
- PI/RC submit amendments, continuing review, adverse events as required
- Study Closeout

5. REFERENCES

Conflict of Interest in Research: *USC policy that addresses financial and other interests that have the potential to compromise research integrity*

<http://ooc.usc.edu/Conflict-Interest-Research>

Certificates of Confidentiality: *Issued by NIH to protect identifiable research information from forced disclosure*

<http://grants.nih.gov/grants/policy/coc/>

ClinicalTrials.gov: *Registry and results database of clinical research studies*

<http://clinicaltrials.gov/>

Collaborative IRB Training Initiative (CITI): *Online training program for Human Subjects Protection, Good Clinical Practice, Responsible Conduct of Research and Conflict of Interest*

www.citiprogram.org

iStar: *IRB electronic submission system*

<https://istar.usc.edu/>

Office for Human Research Protections (OHRP): *Federal entity responsible for protection of research subjects and regulatory oversight of research supported by the US Department of Health and Human Services*

<http://www.hhs.gov/ohrp>

Office for the Protection of Research Subjects (OPRS): *USC Office responsible for protection of research subjects and oversight of USC IRBs*

<http://oprs.usc.edu/>

U.S. Food and Drug Administration: *Federal entity responsible for protecting public health by assuring the safety and efficacy of drugs, devices, biologics, cosmetics, food, and products that emit radiation*

<http://www.fda.gov/>

USC Health Sciences IRB: *IRB responsible for review of studies conducted at the USC Health Sciences campus (mostly biomedical clinical studies)*

<http://oprs.usc.edu/hsirb/>

USC Human Subjects Protection Program (HSPP): *USC Policies and Procedures related to the protection of research subjects*

<http://oprs.usc.edu/rules/>

USC University Park IRB: *IRB responsible for review of studies conducted at the USC University Park campus (mostly socio-behavioral studies)*

<http://oprs.usc.edu/upirb/>

V. PLANNING, DEVELOPMENT AND ACTIVATION OF A CLINICAL TRIAL PROTOCOL

1. Introduction
2. Designing and Writing an Investigator Initiated Clinical Trial Protocol
 - Steps for the Development of an Investigator-Initiated Clinical Trial Protocol
 - Available USC Resources to Assist in Protocol Development
 - Consideration for Participation in Industry Sponsored or Multi-Institutional Consortium Trial
3. Steps for Submission and Activation of a New Clinical Trial Protocol
 - USC Norris Comprehensive Cancer Center Clinical Trial Process
 - Clinical Investigations Committee (CIC) Protocol Review Process
 - Process for Non-Cancer Clinical Trials
 - Clinical Trials Unit (CTU) Protocol Review Process

1. INTRODUCTION

This section is divided into two parts; the first part focuses on the planning and development of an investigator-initiated clinical trial and the second details the steps involved in submitting a new clinical trial for review and approval.

2. DESIGNING AND WRITING AN INVESTIGATOR INITIATED CLINICAL TRIAL PROTOCOL

This part presents a general overview of basic principles that guide the design of clinical trial protocols as well as highlights USC resources available to investigators to support them in this process.

STEPS FOR THE DEVELOPMENT OF AN INVESTIGATOR-INITIATED CLINICAL TRIAL PROTOCOL

a) Define the hypothesis and scientific question(s) to be addressed

A clinical trial is designed to answer a specific question or set of related scientific questions. Having a clear hypothesis and related set of scientific questions is essential to design the clinical trial appropriately and ensure that the experimental plan is well suited to address the questions.

A research question is an interrogative phrase focused on what is to be evaluated by a given research project and what relationships may be established; while a hypothesis is a logical supposition, an educated conjecture that provides a tentative explanation for a phenomenon under investigation. All hypotheses must be based on sound scientific principles and can originate from a variety of sources including a thorough review of the published data, preclinical experiments, and results of pilot studies.

Example:

Research question: Do inhaled corticosteroids reduce asthma hospitalizations in the elderly with co-morbidities?

Hypothesis: Inhaled fluticasone (200 mcg twice a day) compared to placebo reduces asthma hospitalizations in adults greater than 65 years of age with uncontrolled asthma, cardiovascular disease and living in urban settings.

Two tips when formulating a research question and/or hypothesis:

1. It very important that it meets the following criteria: **F**easible, **I**nteresting, **N**ovel, **E**thical and **R**elevant (FINER)
2. It should be as informative as possible so it should include the description of the: **P**opulation, **I**ntervention, **C**omparison group, **O**utcome (PICO).

b) Review internal and external preliminary data to support the hypothesis and justify the conduct of the clinical trial protocol:

Internal data may include preclinical laboratory data from the investigator's laboratory or the laboratory of collaborators or preliminary data from observational studies and/or early phase studies (pilot or Phase I trials). External data may include published literature or preliminary data from outside collaborators including pharmaceutical sponsors.

These preliminary data are critical because they give the investigator an idea of the efficacy (how well an intervention might work) and how safe the intervention being studied is. These data should be summarized with reasonable detail in the background section of the protocol in order to justify the protocol conduct and design. Furthermore, these data are likely to influence the statistical plan because they serve as a reference regarding the expected efficacy and the adequacy of safety information.

c) Define the primary and secondary objectives, general eligibility criteria and overall experimental approach/treatment plan:

The objectives or aims of a study define what will be learned by conducting the research study.

Example:

Objective/Aim 1: To evaluate if the administration of inhaled steroids is effective in reducing asthma related hospitalization in vulnerable populations such as those who are elderly and have specific co-morbidities.

Objective/Aim 2: To evaluate if the administration of inhaled steroids is safe in reducing asthma related hospitalization in vulnerable populations such as those who are elderly and have specific co-morbidities.

Many studies have more than one aim and it is important that all of them be clearly stated in the protocol. It is frequently advisable to have one primary objective and a series of secondary objectives. The statistical plan is carefully developed to address the

primary objective in first place (for example, the sample size is heavily influenced by the primary objective); secondary objectives are also taken into account when developing the statistical plan and some of them may be exploratory in nature.

The research question and hypothesis determine many aspects of the study design such as the population that will be recruited into the study and to which results will be applicable to. Establishing the selection criteria for participant inclusion and exclusion will help the investigator define this population. Inclusion criteria often includes demographic, clinical, geographic, and temporal characteristics while exclusion criteria includes characteristics such as inability to provide certain data, high likelihood of being lost to follow-up, or being at high risk for adverse events. The investigator must give this area of the protocol careful thought because it will also determine key aspects of the study feasibility such as how fast participants can be recruited and how many will accept to participate in the study.

Another aspect of the study that is determined by the research question and hypothesis is the study design used to test the effects and safety of an intervention. Various types of study design can be used ranging from pilot and phase I studies (early phase) all the way to randomized placebo-controlled trial or a randomized equivalence trial. Some of the factors that influence the type of study design include the amount of previous safety and efficacy data that exist regarding a specific intervention, the goal of the study (test initial safety versus establish preliminary efficacy versus establish a new standard of care, etc.). The study design should be clearly described in the methods section of the protocol.

Once the hypothesis, the population and the study design have been selected, a key component that must be described in the methods section is the treatment plan. This plan establishes every detail related to how the intervention will be administered to the participants and includes characteristics such as dose, time per day, duration, etc.

d) Seek statistical consultation to discuss study design

In developing a study design, collaboration with a biostatistician will help to avoid common research pitfalls and help to design an efficient study or experiment to accomplish your research objectives. This can include help with:

- Formulating and/or refining your specific aims and hypotheses
- Identifying and defining key outcomes
- Defining the eligible population
- Planning the statistical analysis / specifying the analytic methods

- Estimating the sample size needed to obtain sufficient power and precision
- Defining the important data elements that should be included in your study/experimental database
- Reviewing the planned conduct of the trial to ensure that it is possible/feasible to obtain the needed data elements

Collaboration with a biostatistician in planning your clinical research can help with the following:

- Does your study design really test your research question?
- Is your study design achievable/doable over the planned study period?
- Do you have special considerations (for example, a rare disease, multiple research sites, non-randomized comparisons of an intervention) that might need some extra thought regarding study design?
- What are some other study design options you might consider that might strengthen your conclusions regarding your research question?
- Are you collecting the right data and at the right time to test your research question?
- Do you have an adequate sample size to validly test your research question?
- Do you have a well thought out plan for statistical analysis that will answer your research question?

e) Perform a feasibility assessment

Thinking in detail about the practical limitations and problems of testing a specific research hypothesis in your setting is a very important process that should be done while designing a research study and documented in the protocol. Understanding the scope of these limits is key in judging the operational feasibility of the study and making necessary changes. There are many reasons why a study may not be operationally feasible, including: inadequate number of participants due to poor recruitment strategies, insufficient technical expertise, inadequate resources (including funding and staffing), or studies that are not affordable in time and/or money.

For each new study, the investigator needs to establish a funding plan to support research related costs that are not considered part of standard medical care, to support the effort of research staff, to fund the performance of assays, and pay for the various administrative costs associated with maintaining the clinical research infrastructure.

The feasibility of conducting a study can also be impacted by the need for an Investigational New Drug (IND) application. Refer to this guidance from the FDA describing when an IND is required:

<http://www.fda.gov/downloads/Drugs/Guidances/UCM229175.pdf>

f) Develop initial application for funding from industry sponsor (Letter of Intent) or grant application

There are various sources of funding available to support clinical research including internal grants, foundation grants, federal grants and pharmaceutical industry sponsors. Since funding availability is essential to the feasibility of conducting a clinical trial, investigators are encouraged to develop a protocol synopsis and include it into a letter of intent (LOI) that can be submitted to the funding entity. The protocol synopsis includes a summary of the main sections of the protocol but in a summarized manner; these sections usually include a background, objectives, eligibility criteria, statistical plan and a section focused on additional assays such as correlative biomarkers.

g) Develop Initial protocol draft

Protocols that are complete and descriptive facilitate the entire process of conducting clinical trials. Investigators should ensure that all essential protocol sections are completed. An important task for a coordinator is to read and re-read the protocol until it is completely clear and become as knowledgeable of every aspect of it as possible. It is a good idea to discuss all protocol specifics and who will perform the tasks involved so that there is a clear delineation of responsibilities.

The essential sections of the protocol are described below. Note that not all studies will require all of these sections, and certain USC entities may require additional items (e.g., the USC/Norris Comprehensive Cancer Center), so it is important to tailor your protocol to your individual needs. Protocol templates are available from both the USC HSC Institutional Review Board and the USC Norris Comprehensive Cancer Center:

IRB: <http://oprs.usc.edu/hsirb/hsirb-forms/>

Cancer Center: <http://uscnorriscancer.usc.edu/Core/CISO/IR.aspx>

1. Protocol Synopsis/Study Summary: Brief overview of the research study question(s), study design, and methodology.

2. Study Objectives: The main aim(s) or hypotheses.

3. Background and Rationale: Discussion of the target disease state for which the investigation holds promise, and any pathophysiology relevant to the potential study treatment action. This section should include a detailed overview of all preliminary data related to the target disease or population and to the intervention. The preliminary data should address available safety and efficacy information. This section should clarify the research question and place it in context of the disease, the population and the current therapies.

4. Investigational Plan/Study Design:

- Type of study: (phase, randomization, double-blind, etc.) Inclusion of a schematic diagram of the trial design, procedures and stages makes understanding the trial much easier for the reader.
- Number of Subjects: Anticipated total number of subjects that will be accrued.
- Study Duration: Length of time each subject will be receiving active treatment and/or will be under observation or follow-up.
- Study Endpoints: Information regarding at what point during the trial primary efficacy will be assessed, safety and tolerability of the investigational product will be evaluated, etc.

5. Selection of Study Population/Patient Eligibility:

- Study Subject Eligibility: Inclusion & Exclusion criteria are criteria that subjects must meet in order to be eligible for study enrollment (e.g. target or concomitant disease, age, gender, etc.).
- Subject Recruitment: How subjects will be recruited for the study (e.g. clinical visits, handouts, ads, phone, chart review, etc.). All advertisements, phone dialogs, and other recruitment materials must be approved by the IRB before use.
- Early Withdrawal of Subjects: The procedure to withdraw subjects, cause of early withdrawal of subjects (e.g. for illness, subject decision to withdraw, etc.), if and how withdrawn subjects will be replaced.

6. Study Drug/Device: Description of the investigative agent, how it appears (e.g. tablets, capsules of __mg), how the drug/device is packaged (amounts, labeling, shipped in bulk, kits, boxes), description of if and how the drug is blinded, how the drug/device is obtained, inventory, procedure for receipt of damaged inventory- notification to the sponsor, description of storage requirements – temperature, light protection, etc., explanation of how the drug/device will be distributed to the research subjects,

including any reconstitution and/or administration requirements, description of any return shipping or destruction of remaining supply instruction, logs, how discrepancies will be handled and resolved.

7. Treatment: Overall description of study required tests and procedures, the Visit Plan may be written in table format and/or written out in words that explains requirements to take place at each study visit. A table format study calendar is very useful in ensuring compliance during study conduct and in facilitating the work of the investigator and research staff (this table may be located in the body of the protocol or added as an appendix/attachment).

8. Data Management: Capture of data generated from conducting the clinical trial may be done in a number of ways. The source of the data is gleaned from the results of tests and procedures, vital signs, clinical notes, flow sheets, questionnaires, etc. and can also be found in source documents. The data are usually later entered into Case Report Forms (CRFs). CRFs may be paper or electronic-based. The assistance of statistician is critical when developing case reports forms since they define the data elements to be captured; the nature of captured data elements and the way by which they are captured has to be consistent with and appropriate for the planned statistical analyses.

- **Logs:** To facilitate study data collection and performance checklists of protocol procedures, a series of logs may be included in this section (e.g., Informed Consent Log, Serious Adverse Event Log, IRB/ Sponsor Correspondence Log, etc.)
- **Confidentiality:** How will subjects' personal information be kept confidential, who will have access to the information, how will it be coded and where will the key for the codes be kept.
- **Data Collection:** The Case Report Form (CRF) is the primary data collection tool for the study. The protocol may have a description of how data will be captured and managed (e.g. electronic versus paper) and how the information will be conveyed to the sponsor, PI, etc.
- **Source Documents:** Original records of clinical findings and observations. Examples: hospital records, clinical charts, laboratory notes, subject diaries, pharmacy dispensing records, x-rays, etc. Copies of source documents must always accompany any CRF or Eligibility Criteria Checklist so as to provide proof of recorded data in case of audit.
- **Record Retention:** Each protocol should have a definitive description of the study record retention plan. This will explain how long study records will be kept after the completion of the trial and what should be done

with them once the required time period is completed (period of time for archiving; destruction after how many years, etc.). FDA-regulated studies must be kept for at least 2 years beyond the formal discontinuation of the clinical development of the investigational product. Non-FDA regulated studies should take into account any applicable Divisional and Hospital requirements.

9. Safety Management

- **Data and Safety Monitoring Plan:** All high risk studies require a Data and Safety Monitoring Plan (DSMP) as a system for appropriate oversight and monitoring of the conduct of the clinical investigation. This oversight ensures the safety of the participants and the validity and integrity of the data.
- **Auditing Procedures:** Explains frequency that the study will be audited and who will perform the audit.
- **Study Stopping Rules:** For high risk studies or those with primary safety endpoints describes procedures for stopping the study. If the study includes a Data & Safety Monitoring Plan, the study stopping rules should be incorporated into the plan.
- **Adverse Events (AE):** The protocol should include a) a description of the expected or anticipated AEs that may occur; b) a Grading Scale used for determining the severity of all possible adverse events; c) an Attribution Scale that helps determine cause; and d) a description of how any adverse events and serious adverse events will be recorded.

For additional assistance in creating a protocol, refer to the publication, “SPIRIT 2013 Statement: Defining standard protocol items” and the associated paper, “SPIRIT 2013 Explanation and Elaboration,” which are available at <http://www.spirit-statement.org/publications-downloads/>

AVAILABLE USC RESOURCES TO ASSIST IN PROTOCOL DEVELOPMENT

a) Design and feasibility consultation meeting

Assistance with protocol development is available to USC investigators through the Clinical Trials unit (CTU) or the Norris Cancer Center Clinical Investigations Support Office (CISO) as part of their “design and feasibility meetings.” These meetings are

typically held in the planning stages of a study (i.e., before seeking funding or IRB approval) and include expert advice in the following areas: protocol design, statistical planning, feasibility analysis, resource utilization and funding strategies. Investigators can request a meeting with the CTU by sending an email to ctu@sc-ctsi.org. Cancer Center members should contact Zeno Ashai in CISO at (323) 865-0463 or Zeno.Ashai@med.usc.edu to schedule a meeting.

b) Biostatistics resources

USC investigators have multiple options for biostatistics help, depending on the nature of the support needed. The Norris Cancer Center Biostatistics Core focuses on cancer studies; the Statistical Consultation and Research Center focuses on genetic-related research and clinical trials, as well as longer term statistical collaborations; and the Southern California Clinical and Translational Science Institute's Biostatistics Program focuses on short-term statistical collaborations (e.g., assistance with study designs, analysis of existing data, etc.). Details about each option, as well as other opportunities for statistical consultation, can be found in the Coordination of Ancillary Services/Support section.

c) Preliminary budget estimate

Clinical Trials Unit (CTU): The CTU can develop a draft budget for CTU-related services if the investigator needs an approximate cost to conduct a trial and is applying for federal funds/grants. This part of the budget only covers the procedures that will be performed at the CTU or with CTU support (such as lab processing or staff resources). The CTU can also draft a Letter of Support to endorse the project.

Clinical Trials Office (CTO): For sponsor-initiated trials, a Budget Specialist in the CTO starts to build USC's first response to the sponsor's proposed budget after receiving the completed coverage analysis. The Budget Specialist works with Principal Investigators, Study Coordinators, department financial administrators, and representatives from other participating units to produce a [preliminary] budget that will facilitate the process of negotiating the budget and payment terms with the sponsor. In addition to completed coverage analyses, the Budget Specialist utilizes the study protocol, sponsor's budget spreadsheet, informed consent, and contract payment terms to complete the development of USC's first budget.

For PI-initiated clinical trials, the Budget Specialist will work with the Principal Investigator to develop a preliminary budget that could be considered by the funding collaborator of the study.

CONSIDERATION FOR PARTICIPATION IN INDUSTRY SPONSORED OR MULTI-INSTITUTIONAL CONSORTIUM TRIAL

a) Complete CDA

A CDA/NDA is used when the owner of confidential information wishes to disclose information to another party, usually in the course of business negotiations, and wishes the information to remain silent. Industry Sponsors typically require a CDA/NDA prior to the release of any confidential information that includes: the Protocol, the Investigator Brochure, all Data, Biological Sample Analysis, and Study Records, Study Budget, and any other information related to the Study, the Company's Drug, or Technology, Research, or Business Plans. By signing a confidentiality agreement, the recipient undertakes the obligation not to disclose the confidential information as defined in the agreement.

The Clinical Trials Office (CTO) is responsible for the review, negotiation, and execution of all CDA/NDA and CTAs on behalf of USC. PIs do not have the authority to execute agreements. Any agreement not signed by an authorized signatory is void.

In many instances, the process of collaboration with industry sponsors begins with the review of their confidential/proprietary information related to a study protocol, drug or a device, or a procedure by an interested USC faculty member. This exchange of information is facilitated through a Confidentiality Agreement. As of this point, this faculty member is identified as the Principal Investigator (PI) representing USC in reviewing the sponsor's confidential information and making a decision about participating in a sponsored-initiated clinical trial. In a PI-initiated clinical trial, the process flow is different, because USC faculty member is the initiator of the study plan/protocol.

Refer to the flow charts in "Contracting, Financial Management, and Budgeting" section, which illustrate the process lifecycle for some of CTO's most frequent activities.

b) Feasibility questionnaire completion

Most industry sponsors and some research consortia ask that the interested investigator at USC completes a feasibility questionnaire; this questionnaire usually focuses on ensuring that the investigator at USC has access to the appropriate study population to ensure adequate accrual and on verifying the presence of an adequate infrastructure for the conduct of the study. It is the responsibility of the investigator to complete the feasibility questionnaire. USC Norris Cancer Center investigators should work with CISO on completing the questionnaire since some sections have standard responses already

developed by the office.

c) Pre-site evaluation visit

The Site Qualification Visit is a meeting conducted to assess the suitability of the investigator and the clinical site. The Site Qualification Visit takes place prior to study submission to Scientific Review Committee (Clinical Investigations Committee CIC) in the case of USC Norris Cancer Center studies and prior to IRB submission in the case of other studies. The Sponsor can request a Teleconference site qualification in lieu of on site visit. In the case of USC Norris Cancer Center studies, CISO coordinates these visits on behalf of the investigators as detailed below:

1. A signed CDA agreement with the proposed PI and the protocol should be supplied to the investigator before or during the qualifying visit.
2. A complete tour of the facilities, Norris Hospital, LAC/USC Medical Center and Keck Hospital of USC including visit to the clinics, infusion areas, Laboratories, Pharmacies (Norris & IDS), Clinical Trials Unit (if applicable), Monitoring room etc.
3. Meeting with the Investigator, Pharmacists (Norris & IDS), and Regulatory team.
4. Protocol submission process and time lines, monitoring visit procedure, study staff contact information etc. The Industry CRA will be provided with the following documents.
 - CIC schedule for the year
 - IRB meeting dates for the year
5. Site Map, Driving direction and lodging information will be provided to the Industry CRA.

3. STEPS FOR SUBMISSION AND ACTIVATION OF A NEW CLINICAL TRIAL PROTOCOL

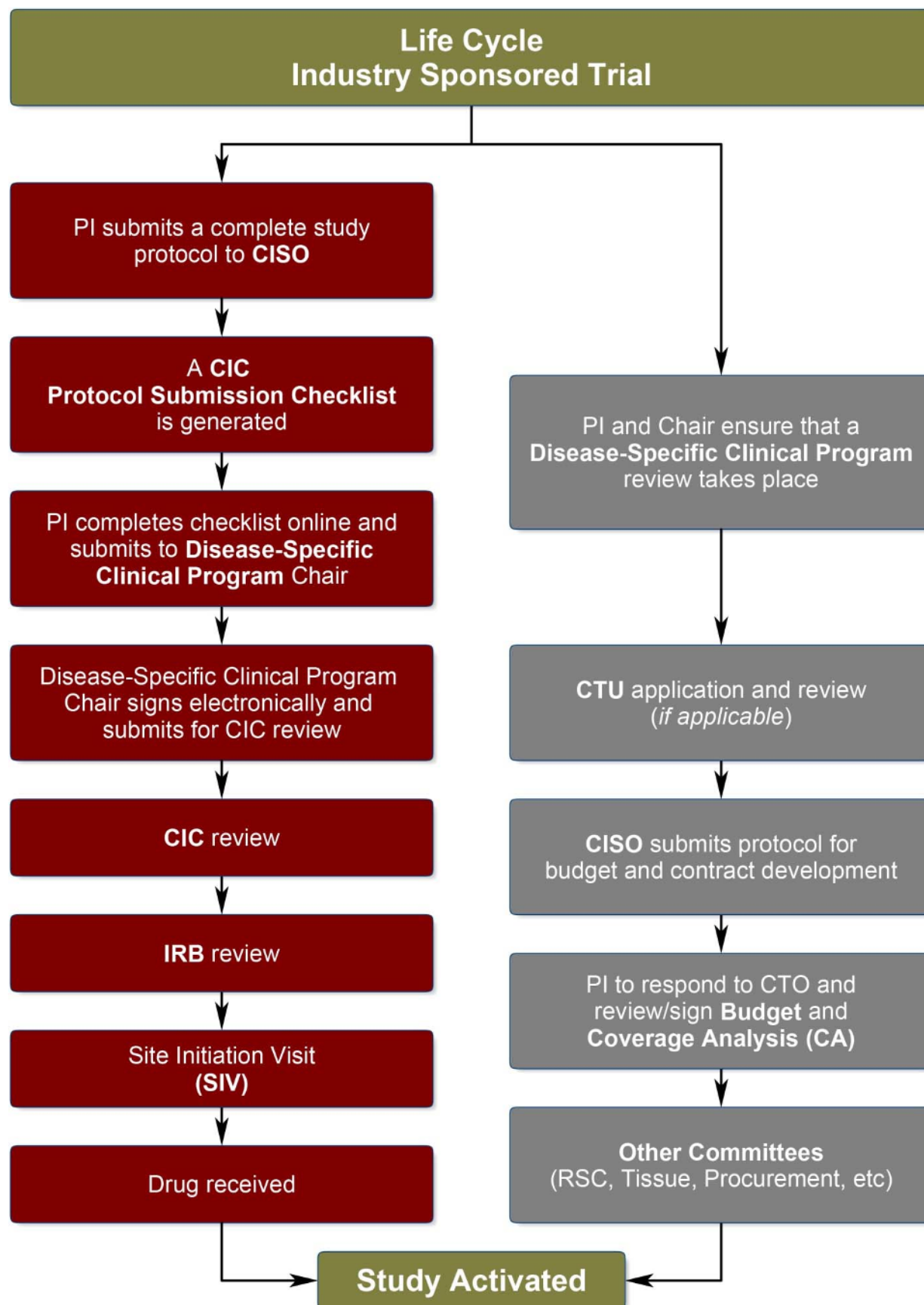
USC NORRIS COMPREHENSIVE CANCER CENTER CLINICAL TRIAL PROCESS

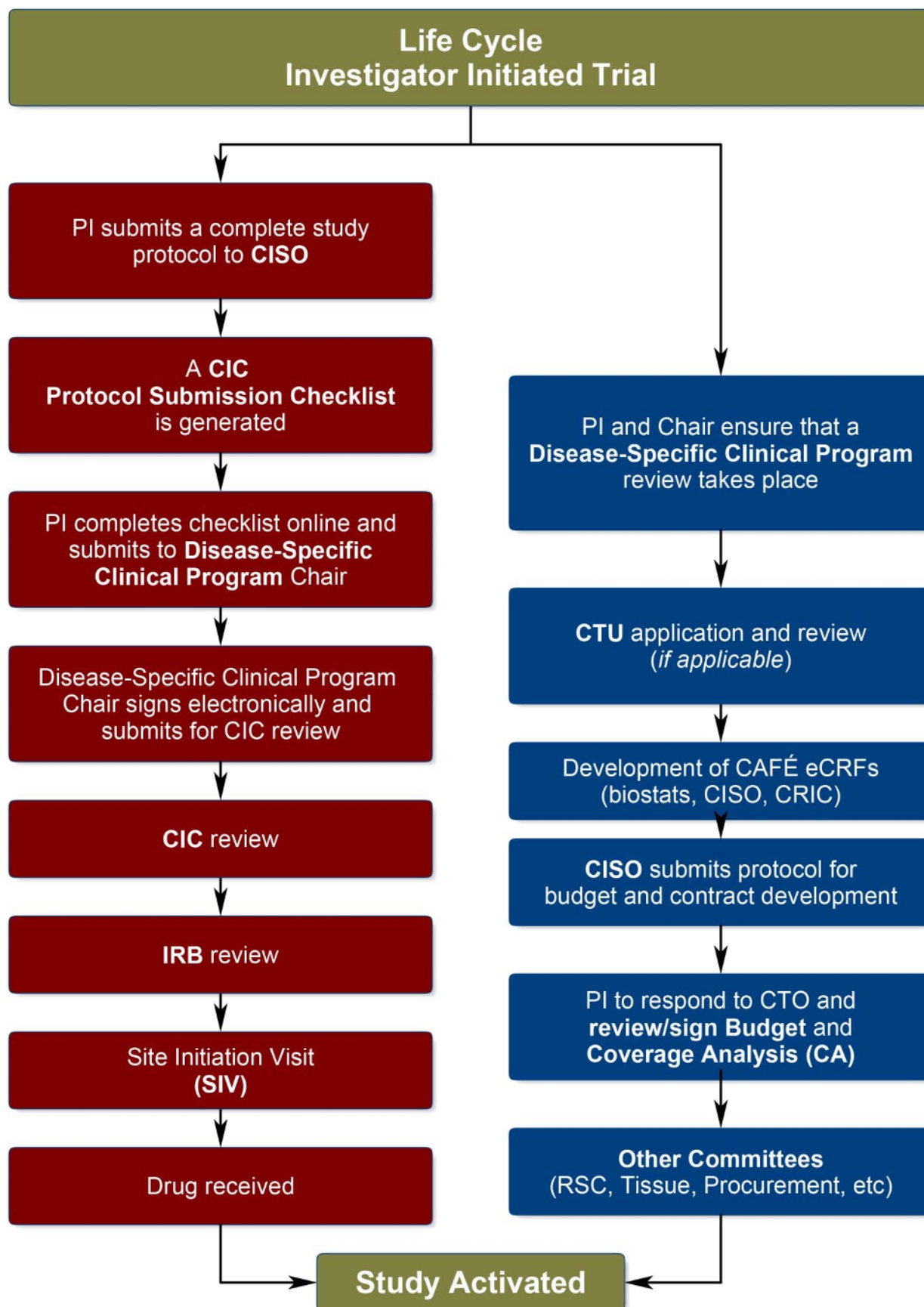
ALL clinical and translational protocols at USC that involve human subjects and are designed to address a cancer focused scientific question must be reviewed and approved by the Clinical Investigations Committee (CIC) prior to IRB review and approval. The cancer focused scientific question may be related to cancer diagnosis, screening, prevention, or treatment. The USC Norris Cancer Center Clinical Investigations Support Office (CISO) serves as the single point of entry for all cancer

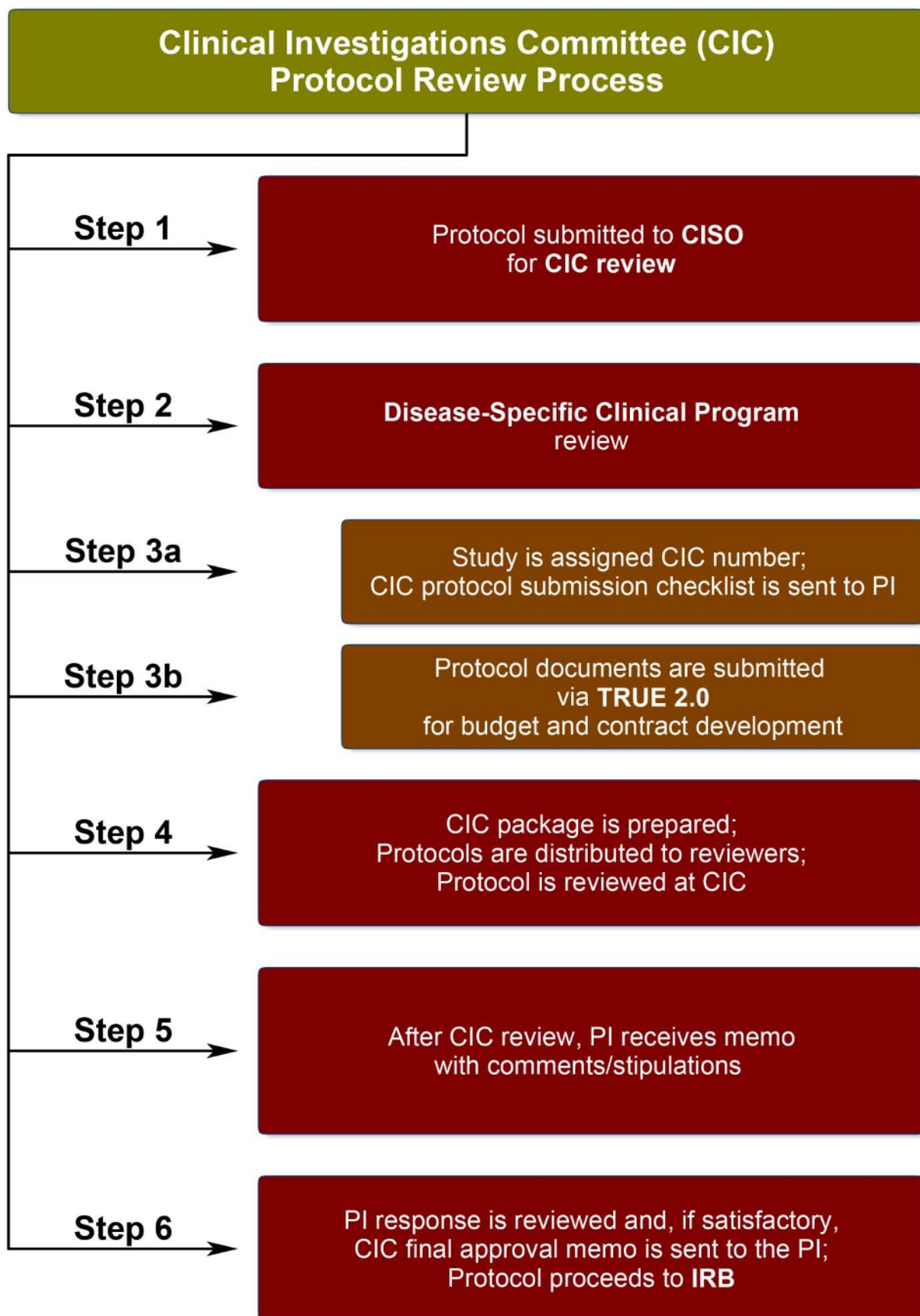
related protocols and centrally manages the process of study review and activation (including submission of the protocol to CTO for contract and budget development).

The following flowcharts pertain to Cancer Center members who are submitting a new protocol for review. CISO has an investigator guide/manual which can be accessed at:

<http://www.uscnorris.com/Core/CISO/IR.aspx>







CLINICAL INVESTIGATIONS COMMITTEE (CIC) PROTOCOL REVIEW PROCESS

Step 1: Protocol submissions

Protocols are reviewed by the CIC twice a month (1st Wednesday and 3rd Thursday). The deadline for submission of new protocols and re-submitted protocols to the CIC is the 2nd and 4th Friday of the month prior to the next month's Wednesday and Thursday meetings respectively. CIC meeting schedule and submission deadlines are available at <http://uscnorriscancer.usc.edu/Core/CISO/ViewPending.aspx> (password protected).

A complete manual for CIC submission, member information is available at <http://uscnorris.com/core/cic.aspx>.

No more than ten (10) protocols can be reviewed per meeting, so protocols will be processed on a first-come first-served basis.

Submit your protocol along with the informed consent, investigator brochure, and any other related documents (such as sponsor budget, CDA, etc.) to the CIC coordinator at CIC@med.usc.edu. You can also submit it to Zeno Ashai or Criselda Chang. They can be contacted at zeno.ashai@med.usc.edu or chang_c@med.usc.edu.

Step 2: Disease-Specific Clinical Program Review

The Disease-Specific Clinical Program Review is a required step to ensure that there is programmatic buy-in and support for the study. Documentation of this review is included in the CIC Protocol Submission Checklist. The Chair of the Disease-Specific Clinical Program signs off to verify that the Disease-Specific Clinical Program review has occurred.

Step 3a: Completion of CIC Protocol Submission Checklist

On receipt of protocol, the investigator will get an email to electronically complete and submit CIC Protocol Submission Checklist. **Without a completed Checklist, there can be no further progress, and the protocol will not go to CIC or CTO.**

Step 3b: Contract & Budget Development

The CISO Business Manager submits the protocol documents via True 2.0 for budget and contract development. CTO will not start budget & contract process without the CIC Checklist.

Step 4: CIC Review

Protocol Distribution prior to CIC Meeting

Complete study package which includes Protocol, Sponsor and USC formatted ICF, CIC PSC, is sent a week before the meeting to assigned reviewers and CIC members who are required to attend the meeting. Reviewers must respond within 24 hours if they are unable to do the review. The deadline for submission of reviews is a day before the CIC meeting.

CIC will defer protocols if all reviews are not received on time for CIC review.

There are two types of CIC reviews:

- *Full review*: Each study undergoes scientific and operational review. Two peer-reviewers, one statistician and one operational reviewer from CISO are assigned to review the protocol.
- *Modified review*: Cooperative Group, NCI CTEP reviewed and sponsored, and specimen studies, all require one peer-reviewer and one operational reviewer to conduct a modified scientific review. The review is focused on study feasibility and prioritization.

CIC Correspondence after the CIC meeting to the Investigator. Within a week from CIC review, the investigator will receive a memo with comments/stipulations from the CIC.

Step 5: Response to the CIC

The PI is expected to respond to the CIC stipulations within one month of receiving the memo. The PI may request an extension of an additional two months. An automatic reminder is sent to the investigator every 15 days.

If the PI does not respond, the study will be placed in the “closed file”. To reopen the study, the PI will be required to complete a new protocol submission and start the entire process of CIC review again, as if submitting a new study.

Stipulation from CIC Requiring Approval by Designated Reviewers

After the Investigator has responded to the stipulations, the CIC Coordinator sends the Investigator’s response to designated reviewers who will have up to 2 weeks to review, approve/ disapprove and return to CIC coordinator. If a response is not received an automatic reminder is sent at the end of 1 week and then daily past 2 weeks until a response is received.

Step 6: CIC approval

If the PI's response to stipulations is satisfactory, the PI will receive a final approval memo from the CIC.

IRB Submission

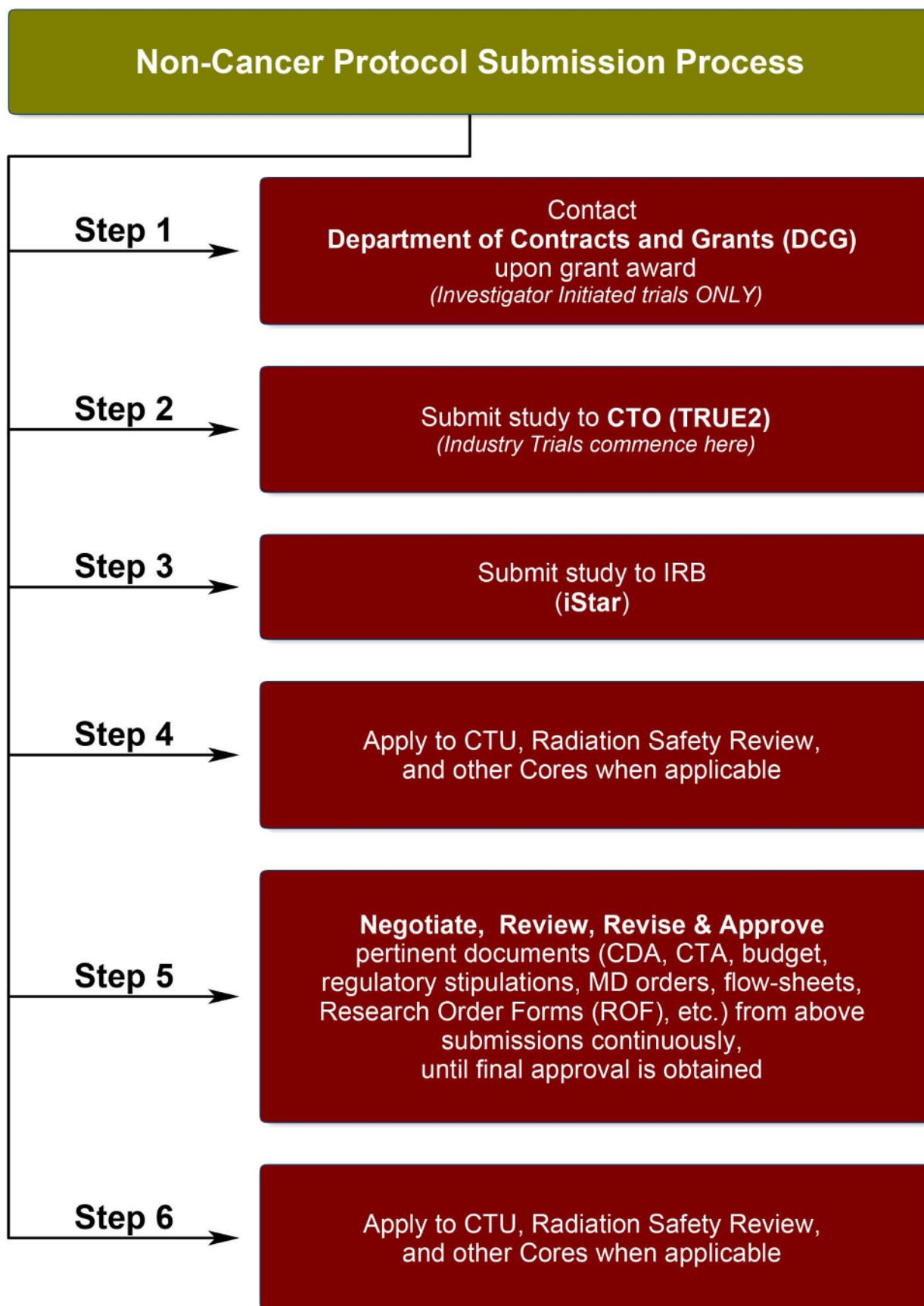
After all CIC stipulations have been approved by the Co-chair, the appropriate Regulatory Manager will start IRB submission within 2 weeks. This timeline depends on Sponsor approval of Informed Consent and signed lab agreements, etc.

PROCESS FOR NON-CANCER CLINICAL TRIALS

As of September 2013, clinical trials outside of the USC Norris Comprehensive Cancer Center are managed through the submission and review process by the investigator and study team. Some departments have begun to institute a centralized clinical research operation/office such as the Department of Surgery which launched a division of clinical research.

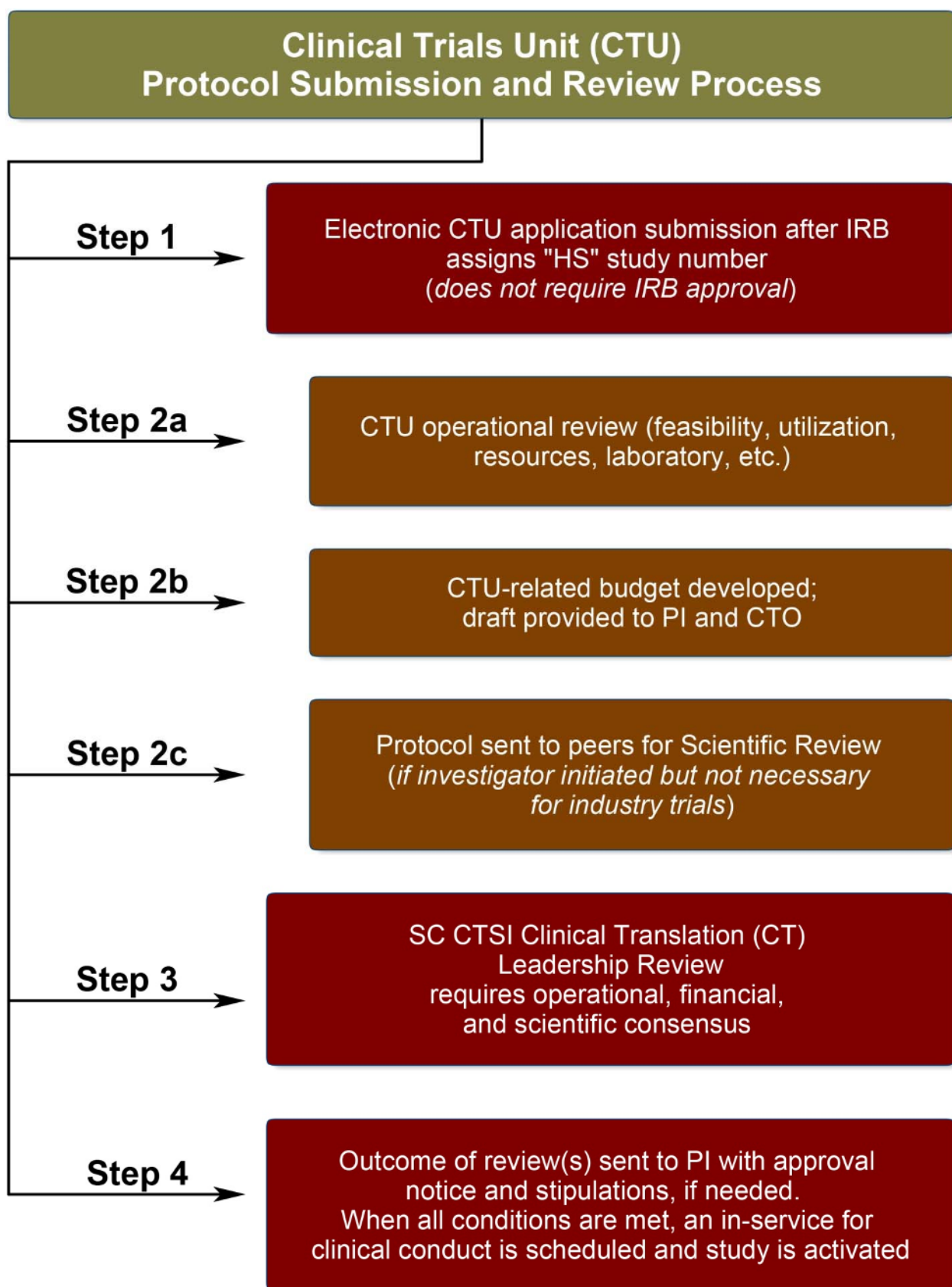
The steps involved in the submission of a clinical trial for review and approval outside of the USC Norris Comprehensive Cancer Center are the following:

- 1- Submit all clinical trials documents (protocol, CTA, external budget if provided) in TRUE2 to CTO
- 2- Investigator initiated trials or trials with grant support (other than industry) have to also be submitted to Department of Contracts and Grants to set-up the award.
- 3- In parallel to step 1 and/or 2, the protocol can be submitted to IRB via iStar. Studies that need to use the Clinical Trials Unit (CTU) may be submitted to CTU in parallel to the IRB review (see below).
- 4- The PI and study team will interface with CTO regarding the coverage analysis and the budget/contract; they will also interface with IRB to address the IRB stipulations.
- 5- Once the budget and contract are completed and approved, final IRB approval is granted once the consistency checklist is completed by CTO.
- 6- In the case of investigator initiated studies, investigators are encouraged to ensure that they have determined the data capture system that they will use and develop the Case Report Forms (CRFs) to ensure accurate data entry. "Redcap" is a useful data capture system under the CTSI.
- 7- Patient recruitment should not start until the investigational product is received at USC and the research order forms (ROFs) are posted.



CLINICAL TRIALS UNIT (CTU) PROTOCOL REVIEW PROCESS

Investigators wishing to request Clinical Trials Unit infrastructure, resources, and/or support to conduct human studies must complete the online CTU application. The complete process takes approximately 45 days, from day of submission to approval/dissent notice (see next page).



Step 1: Submit CTU Application Online:

The application may be submitted prior to IRB approval but requires an “HS” (Human Subjects) number. It is highly recommended that investigators submit their protocols to the CTU shortly after IRB submission so that both reviews are done in parallel, thereby reducing time to study start. Please gather the following information and/or documents to complete the online application:

- IRB information
- Utilization dates
- Lab manual or specimen processing guidelines, if service requested
- MD orders
- Schedule of Services spreadsheet for non-industry studies only
- CISO documents for Cancer Center members only
- Identify visits in which CTU services are being requested

There are 7 sections in the CTU application, including a starter page, 5 study-specific modules, and the submission summary. It may take up to one hour to submit the CTU application but you do not have to complete it all at once. You may choose to save the entered data per module and return at a later time to resume and/or complete it. However, you will not be able to modify, add, or change any data in the application once submitted.

Instructions:

- Go to website <http://SC-CTSI.org/>
- Locate the "Resources" tab on the toolbar
- Select "Conduct Human Studies and Trials"
- Click on USC CTU Online Application at the bottom of the page
- Select your institution: USC
 - USC NetID Username and Password required
- Complete and submit application

At the end of the submission, the PI will receive an automatically generated e-mail confirming the application was successfully completed. A second notice is sent when the application is received and reviewed by CTU administration with instructions for next steps and pertinent timeframes.

Step 2a: Operational Review

The protocol is distributed internally at the CTU to Supervisors and Managers in their

respective field of work for feedback on clinical operations, laboratory procedures, and nursing. Operational review occurs upon receipt of CTU application and all study-related documents.

Step 2b: CTU-specific budget development:

A budget is drafted for CTU-related services and provided to both, the PI and the Clinical Trials Office. The excel spreadsheet is inclusive of all infrastructure costs for the activities and procedures occurring at the CTU per visit, including space, nursing time, meals, essays, supplies, etc. The worksheet also states administrative fees, if any, as well as subsidy percentage when applicable.

Step 2c: Scientific Review:

All studies require scientific review. However, industry trials or PI-initiated studies that have undergone external peer review by a qualifying authority are exempt if a written report such as the summary statement from NIH study section or Cancer Center Clinical Investigation Committee notice of approval is provided. If the external review cannot be provided, the CTU will conduct an internal scientific peer review by one or two reviewers and a designated statistician. The reviewers may be members of the CTSI Clinical Translation Leadership Committee, faculty, and/or expert in the proposal-specific research filed.

Scientific peer review has dual focus; to determine scientific quality as well as fiscal and operational feasibility of conducting the study at the CTU and/or with CTU support. The review will also address whether the study is consistent with the overall CTSI mission and goals.

Step 3: SC CTSI Clinical Translation (CT) Leadership Review:

The outcomes of the operational and scientific peer review (when needed), as well as the costs associated with the study are presented and discussed at a Clinical Translation Leadership Committee meeting. The group meets monthly, on the third Tuesday of every month, and decides whether or not the clinical trial may be done at the CTU and/or will be supported by SC CTSI.

Step 4: Outcome of Review(s) Notice to PI:

A notice of approval or dissent is sent to the PI within 3 business days of the CT Leadership Committee voting result. More often than not, approval is granted with contingencies and the investigator is required to address all stipulations before scheduling the first research participant for a CTU visit.

VI. COORDINATION OF ANCILLARY SERVICES/SUPPORT

1. Introduction
2. Radiology & Imaging
 - Radiology
 - Molecular Imaging Center (MIC) - Radiochemistry/Cyclotron Labs
 - Molecular Imaging Center (MIC) - Small Animal Imaging Core
3. Pharmacy
4. Pathology
5. Clinical Trials Unit
6. Biostatistics
7. Cardiology
 - CardioVascular Thoracic Institute (CVTI) or KECK Hospital of USC
 - Echo Core Lab
8. Ophthalmology
9. Primary Contacts for Accessing Ancillary Services or Support

1. INTRODUCTION

The compliant conduct of high quality clinical research requires the availability of an efficient and accessible infrastructure. Frequently, many services provided through this infrastructure are not under the research team's control; however, it is important that the research team be familiar with how the services function, their requirements, their challenges, and their processes. Similarly, the academic center leadership has the responsibility to ensure that the infrastructure services are in tune with the clinical research needs and rules. This section is intended to provide an overview of the ancillary and support services needed for the conduct of clinical research at USC.

2. RADIOLOGY & IMAGING

Imaging plays an important role in clinical research for multiple reasons. It may be used to assess response to treatment in cancer patients, to evaluate changes in metabolic parameters such as bone density, or as a surrogate of physiologic changes at the cellular level in the case of functional imaging such as a PET scan. If your clinical trial protocol includes research-related imaging, it is important that you contact the research administration within the Department of Radiology to make the necessary arrangements. Below is a list of services provided by Radiology and the Molecular Imaging Center and an outline of the processes that need to be followed.

RADIOLOGY

- **Overview of services provided**

Services are available at the Norris Cancer Center and at Keck Hospital (Healthcare Consultation Center II and the PET Center in Healthcare Consultation Center I). Patients recruited from Los Angeles County Hospital may be imaged at HCC2 or the PET center only if funding is available. For research studies that will utilize radiology services at Keck, the procedures described below should be followed.

- **How can researchers utilize the services provided?**

Typically, the coordinator will send an email to Bhushan Desai (bhushand@usc.edu; 323-865-9949) or contact the [Department of Radiology](#) (323) 442-8541, outlining the imaging requirements for the study and provide any additional materials (i.e., imaging manual). You can request imaging using the Research Order Form created by the Clinical Trials Office.

- *What is the process in place to access the services?*
 - A) If special imaging is required by the research protocol, a meeting between the Chief Technician, research staff and PI **should** be scheduled to discuss the requirements & feasibility of the imaging portion of the study (i.e., 3D rendering, special sequencing, required training of technologists, etc.). B) A Radiology Research Agreement form must be submitted to set up the protocol in the Radiology department. The form can be obtained from Bhushan Desai (bhushand@usc.edu; 323-865-9949) or from the [Department of Radiology](#) (323) 442-8541). C) Radiology will then create a Radiology Scan Request form that must accompany the Clinical Trials Office (CTO) created Research Order Form (ROF) when scheduling the subject for a research imaging procedure.
 - Radiology will email the investigator/research coordinator a Radiology Scan Request form specific for their study. This form identifies the imaging protocol for the technician to follow to assure all research subjects are scanned according to protocol. This form must be completed with subject information each time a subject is scheduled at the Healthcare Consultation Center II (HCC2) Lower Level or the PET Center located on the 3rd floor of the Healthcare Consultation Center I (HCC1).
 - If Radiology imaging services will be done at either Keck Hospital or Norris Cancer Hospital, a Radiology Scan Request form is not required. A ROF will suffice to schedule the radiology service.
 - If the imaging is done per standard of care/non-investigational (no research images needed, no special sequencing, etc.) then a Research Agreement is not required. A ROF will suffice to schedule the radiology service. The ROF should not be used for non-study related tests or procedures, such as routine care. If there is a routine service that is needed outside of the study protocol, please order utilizing the standard clinical ordering process. A Radiology Research Agreement form is only required when requesting specialized imaging (e.g., 3D rendering, special sequencing) at HCC2 or the PET Center.
 - Please note: If both technical (scan only) and professional (read by a radiologist) services are required by Radiology for the research scan, you will receive two bills: one bill from USC for the technical scan service and

a separate bill from USC Care Medical Group for the professional scan read.

- Radiology does not upload research images to sponsor websites. Uploading images is the responsibility of the study team. Radiology will prepare an anonymized CD for the study team to pick up, if requested before the scanning begins.

- *Who initiates the process?*

Coordinators, research staff or physicians can contact Bhushan Desai (bhushand@usc.edu; 323-865-9949) or the [Department of Radiology](#) (323) 442-8541 for instructions.

- *When should the process be started?*

The process can be initiated while the study is under review by the IRB. However, no research scans may be scheduled until the study has final IRB approval, ROF is available and Radiology Scan Request form (if applicable) is completed.

- *Are there differences in the process between Keck Medical Center and LAC+USC?*

The process described above only applies to research imaging conducted at HCC2 and the PET Center located at HCC1. Patients recruited from Los Angeles County Hospital may be imaged at HCC2 or the PET center only if funding is available.

- **What are the charges involved?**

Radiology research imaging charges are determined by the coverage analysis performed by the Clinical Trials Office (CTO). Please note – There is a charge of \$330 by the Department of Radiology for completion of RECIST tumor flow sheet form by a radiologist. Please make sure CTO is aware and prepares your budget accordingly.

- **List of contacts for the service/core, [click here](#).**

Bhushan Desai
bhushand@usc.edu
323-865-9949

Edward Grant, MD, Chairman

edgrant@med.usc.edu

323-442-8541

Sam Valencerina, Chief Technician

Samuel.valencerina@med.usc.edu

Researchers are encouraged to contact appropriate Radiology faculty for consultation and assistance with research imaging. Click [here](#) for a list of our divisions/division chiefs.

- Body Imaging: Suzanne Palmer (Suzanne.Palmer@med.usc.edu)
- Abdominal Imaging/Oncologic Radiology: Vinay Duddalwar (Vinay.Duddalwar@med.usc.edu)
- Thoracic/Cardiac Imaging: Alison Wilcox (Awilcox@med.usc.edu)
- Ultrasound: Edward Grant (Edgrant@med.usc.edu)
- Interventional Radiology: Michael Katz (Michael.katz@med.usc.edu)
- Musculoskeletal Radiology: Eric White (Eric.White@med.usc.edu)
- Neuroradiology: Meng Law (Meng.law@med.usc.edu)
- Nuclear Medicine/PET: Robert Henderson (Rhenders@med.usc.edu)
- Women's Imaging: Linda Hovanessian Larsen (Lhlarsen@med.usc.edu)

MOLECULAR IMAGING CENTER (MIC) – RADIOCHEMISTRY/CYCLOTRON LABS

- **Overview of services provided**

There is an ever-increasing demand for new and more sophisticated imaging probes for experimental research and clinical application, especially with the escalation of molecular medicine approaches to therapy design. The MIC has created a rich environment for research and clinical studies with molecular imaging. It is equipped with a new state-of-the-art cyclotron and radiochemistry laboratories. It has three full-time radiochemists and a number of staff members. Researchers with access to MIC can now make significant contributions, particularly in the area of clinical interests from oncology, cardiology, to neurology. The center can develop and validate novel molecular imaging probes (organic molecules, peptides, antibodies, proteins, and peptidomimetics) for clinical research. Examples include studying the angiogenesis process using radiolabeled RGD peptides (^{18}F -FPRGD2, ^{18}F -FPRGD4, ^{64}Cu -DOTA-RGD4, ^{68}Ga -NOTA-RGD multimer, $^{99\text{m}}\text{Tc}$ -MAG3-RGD multimer) for microPET of tumor $\alpha_v\beta_3$ integrin expression (^{18}F -FPRGD2 are being tested in clinical trial at Stanford

University); investigating cell proliferation indicators (^{18}F -FLT, ^{11}C -/ ^{18}F -FMAU); studying Alzheimer disease (^{18}F -PIB, ^{18}F -AV-45) and hypoxia (^{18}F -FAZA, ^{18}F -FMISO and ^{64}Cu -ATSM); performing reporter gene based imaging (^{18}F -FHBG); studying Dopamine receptors using ^{18}F -Fallypride and ^{18}F -FDOPA; and evaluating cardiac disease with MPI PET agents. As shown in Table 1, a broad range of radiotracers will become available for clinical use.

Table 1: Partial List of positron-labeled radiotracers that can be produced

Radiotracers	Usage
Na^{18}F	Bone imaging
H_2^{15}O	Blood flow imaging
$^{13}\text{NH}_3$	Cardiac imaging
^{18}FDG	Oncology
^{18}FU	Oncology
$^{18}\text{FHBG}$	Reporter gene imaging
$^{18}\text{FHPG}$	Reporter gene imaging
$^{18}\text{FIAU}$	Reporter gene imaging
$^{18}\text{FBAU}$	Reporter gene imaging
$^{18}\text{FCAU}$	Reporter gene imaging
$^{18}\text{FMAU}$	Reporter gene imaging/oncology
$^{18}\text{FEAU}$	Reporter gene imaging/oncology
$^{18}\text{FFAU}$	Reporter gene imaging/oncology
$^{18}\text{FB-RGD}$	Angiogenesis imaging
^{18}FLT	Oncology
$^{18}\text{F-MISO}$	Hypoxia imaging
$^{18}\text{F-Fallypride}$	Brain imaging
$^{18}\text{F-DOPA}$	Brain imaging
^{18}FXA	Cardiac imaging
^{18}FAA	Spleen imaging
$^{11}\text{C-choline}$	Oncology
$^{11}\text{C-FMAU}$	Oncology
$^{11}\text{C-Acetate}$	Oncology
$^{11}\text{C-PIB}$	Alzheimer's
$^{64}\text{Cu-PTSM}$	Hypoxia imaging
$^{64}\text{Cu-RGD}$	Angiogenesis imaging

- **How can researchers utilize the services provided?**

Researchers interested in utilizing these services should contact MIC to set up an initial meeting with the lab manager, Grant Dagliyan (dagliyan@usc.edu), and one of the radiochemists. This initial meeting should be set up as far in advance as possible, in

order to assess the feasibility of the study and the radiotracer. There are no differences in the process if a study is conducted at Keck Medical Center and LAC+USC.

- **What are the charges involved?**

Costs for the production of the radiotracers vary and will be discussed during the initial meeting.

Click [here](#) for a list of contacts for the service/core or contact

Madlen Aladadyan, Program Manager

maladady@usc.edu

323-442-3858

Grant Dagliyan, Lab Manager

dagliyan@usc.edu

323-442-1166

MOLECULAR IMAGING CENTER – SMALL ANIMAL IMAGING CORE

- **Overview of services provided**

MIC's Small Animal Imaging Core is dedicated to research studies of small animals for a variety of applications. The Core facility is staffed with trained machine operators and animal technologists. MIC faculty are active in developing novel methods of imaging to obtain new types of information as well as in applying current methods to study a wide range of biomedical questions. The pre-clinical versions of PET, CT, and ultrasound scanners in our facility provide information from studies in pre-clinical models, which can be directly translated to clinical settings. In addition to the structural and functional data provided by each instrument mentioned above, supplemental data can also be acquired using autoradiography and biodistribution studies. In addition, optical imaging studies provide gene reporter analysis using transgenic models or tumor cell lines with luciferase or fluorescence measurements of labeled molecule distribution using quantum dot nanotechnology.

- MicroCT
- MicroPET
- Micro-Ultrasound
- Optical Imaging

- Quantitative Autoradiography
- Digital Radiography
- **How can researchers utilize the services provided?**

Researchers interested in utilizing these services/instruments should contact MIC to make an appointment for imaging. Reservations should be made 2 weeks in advance, but last minute reservations will also be taken, if equipment is available. There are no differences in the process for researchers at Keck Medical Center and LAC+USC.

- **What are the charges involved?**

Prices are listed below. Norris Cancer Center members receive a 20% discount and School of Pharmacy faculty receive a 10% discount.

MicroCT:	\$150/hr
MicroPET:	\$200/hr
Ultrasound:	\$150/hr
Optical Imaging:	\$130/hr
Digital Autoradiography:	\$125/hr
Faxitron (plain film studies):	\$30/exp
Radioisotope/Contrast Agents:	call for price
Post-Processing/Image Analysis:	\$50/hr

- Click [here](#) for a list of contacts for the service/core

Madlen Aladadyan, Program Manager
maladady@usc.edu
323-442-3858

3. PHARMACY

- **Overview of services provided**

The Investigational Drug Services pharmacy supports human clinical research involving study drugs and supports safety and care for research participants in both the inpatient and outpatient care areas. The Investigational Drug Services pharmacy integrates its activities with the clinical, safety, informatics, administrative, and drug distribution systems of the hospitals and clinics to optimize study drug therapy for patients.

The investigational drugs services pharmacy offers:

- Regulatory compliance
 - Integrity of blinding
 - Prevention of errors involving study drugs dispensing and accountability
 - Dispensing of investigational products in a timely manner
 - Contribution to study design and data integrity
 - Randomization and study drug accountability
 - Sterile preparation and distribution of both hazardous and non-hazardous study medications in a USP 797-compliant environment
 - Drug and supply procurement as needed
- **How can researchers utilize the services provided?**
 - *What is the process in place to access the services?*

Pharmaceutical Investigational Drug Services are supported by three pharmacies and can be used to support research at Keck Hospital of USC Inpatient, Keck Hospital of USC Ambulatory Clinics, LAC+USC Hospital, and Norris Cancer Center. Services are provided through the standard medication process of each site. Investigators should contact Caroline Chellamy (chellamy@usc.edu, 323-865-3545) for pharmacy services at the Norris Cancer Center, the Clinical Trials Unit, or Keck Hospital of USC, LAC+USC and all other sites.
 - *Who initiates the process?*

The request for Investigational Drug Service support can be initiated by the Principal Investigator and his or her designee.
 - *When should the process be started?*

The process may be started prior to the protocol being submitted to the IRB for review, or at the latest, in parallel to the IRB review. Ideally, if the protocol involves a study medication the Investigational Drug Service should be contacted as soon as possible to facilitate compliance, operational, and budget requirements.
 - *Are there differences in the process between Keck Medical Center and LAC+USC?*

No.

- **What are the charges involved?**

<u>Fixed Fees</u>	
Pharmacy	\$1,000
Termination (Closeout)	\$500
Annual Storage and Monitor Visits	\$1,000
<u>Dispensing Fees</u>	
Chemotherapy IV	\$100
Chemotherapy IV – Off Hours	\$150
Non-Chemotherapy IV	\$65
Oral (per pt/dispense)	\$30
Oral (per pt/dispense) – Off Hours	\$45
IV Bolus	\$45
IV Bolus – Off Hours	\$68
Randomization (one time per patient)	\$90

If investigational drug is not provided by the sponsor, then the cost of the drug will also be charged to the investigator's budget.

List of contacts for the service/core or the [Norris Cancer Center](#), the Clinical Trials Unit or LAC+USC Hospital and Keck Hospital of USC's Ambulatory Clinics or Keck Hospital of USC

Caroline Chellamy, Pharm.D., Director of Ambulatory Pharmacy Services,
Pharmacist in Charge, USC I.D.S. Pharmacy
IDSParmacy@med.usc.edu
323-865-3538

4. PATHOLOGY

- **Overview of services provided**

The point of entry for all biospecimen procurement needs is the Translational Pathology Core Facility (TPCF) of the USC /Norris Comprehensive Cancer Center, whether for clinical trials or non-interventional translational research studies, and whether cancer-related or not. In this capacity, the TPCF works closely with the hospital-based employees of the LAC+USC Medical Center and the Keck Medical Center to facilitate the process of research tissue acquisition and processing and to insure compliance with federal, state, and local hospital regulations. The activities of the TPCF are supported by

chargebacks to the principle investigator on the study. Any investigator may request services from the TPCF; Cancer Center members receive services at a discounted rate. Click [here](#) for the list of charges for various services provided by the TPCF.

- **How can researchers utilize the services provided?**

i. For all research studies requiring the use of human biospecimens, including both Clinical Trials and non-interventional (non-Clinical Trial) translational research studies (see below), after funding and IRB approval have been obtained, investigators must submit one of two forms to TPCF in order to obtain approval to procure biospecimens: either Application for Tissue and/or Fluid for Research for procurement from Norris or Keck Hospitals or LAC+USC Lab Agreement for procurement from LAC+USC Hospital. Both forms can be obtained from and submitted to Mo-Li Chen, Supervisory Technologist (mhchen@usc.edu). Once the Application/Lab Agreement is approved, the investigator will meet with Ms. Chen to arrange the implementation of the biospecimen procurement, processing, and distribution required by the protocol.

ii. Once the research protocol is initiated, two additional forms will enable investigators to request procurement from individual patients: Request for forms for FFPE Slides/Tissue Blocks and Request for Fresh/Frozen Tissues can also be obtained from and submitted to Ms. Chen

iii. For non-interventional (non-Clinical Trial) translational research studies, it is strongly recommended that the principle investigator (PI) or his/her designee meet with either Dr. Sue Ellen Martin (Director, TPCF) or Dr. Andy Sherrod (Co-director, Adult Tissue Arm) as early as possible in the planning process to discuss the design of the study (i.e., before submitting to funding agency or IRB). The purpose of this meeting is to assure that the required biospecimens will be available for the study and that adequate funding will be budgeted to pay for biospecimen procurement and processing. The meeting can be arranged by emailing Dr. Martin and copying Dr. Sherrod and their assistant Gina Madrid. Investigators initiating clinical trials do not need to have this initial meeting.

- **Types of human biospecimens available for research**

i. Formalin-fixed, paraffin-embedded (FFPE) tissues:

All tissues taken during the course of clinical care are saved for a period of time in the hospital archives in the form of FFPE blocks. These can be used for research purposes provided appropriate consent and IRB approval have been obtained. At Keck Medical Center, these tissues are stored indefinitely. At LAC+USC, the FFPE tissues are stored in

the hospital archives for 10 years, at which point they are donated to the Population Based Tissue Arm of the TPCF. TPCF personnel can assist with procurement and sampling (e.g., sectioning, coring) of FFPE blocks in the hospital archives.

ii. Fresh, fresh/frozen, and fluid specimens (e.g., whole blood, serum, plasma, buffy coat, and urine):

Fresh, fresh/ frozen and fluid biospecimens can be collected prospectively for IRB approved, funded studies with a valid Lab Agreement and patient Informed Consent. Typically both tumor and matched normal tissue are collected immediately after explanation under the supervision of the service pathologist. The TPCF will assist with the immediate processing and storage of the specimens, banking and tracking of the specimens, and distribution and processing required for analysis.

- **Who can obtain specimens?**

Specimens can be obtained by USC investigators with IRB approved, funded studies with a valid Lab Agreement.

- **Processing capabilities**

Processing capabilities include procuring hematoxylin & eosin (H&E) stained slides and FFPE blocks, embedding tissues in paraffin, thin sectioning (5 μ), thick sectioning, and ribbons of blocks, coring blocks, preparing tissue microarrays, and preparing buffy coat and ficoll-hypaque separations. Click [here](#) for contact information for the core.

- **Additional resources**

An additional source of FFPE tissue is the Residual Tissue Repository (RTP) (Wendy Cozen, DO, MPH, Director), a valuable population-based tissue repository consisting of cancer cases pulled from the Population Based Tissue Arm donations, as well as blocks from over 30 other regional hospitals. The samples are linked to the Surveillance, Epidemiology & End-Results (SEER Program) to obtain corresponding clinical and demographic data (non-patient identifiable information). The RTP is the largest multi-ethnic resource of its kind, with 500,000 FFPE blocks from 65,000 cancer patients. Provided the investigator has an IRB approved protocol, approved Lab Agreement, and funding, the TPCF personnel will assist with procurement and sampling (e.g., sectioning, coring) of FFPE blocks in the RTP.

The TPCF also supports basic research through procurement and processing of animal tissues. For further information, contact Dr. Martin or Dr. Sherrod.

- List of contacts for the service/core, click [here](#) or email CoreTransPath@med.usc.edu

Sue Ellen Martin, MD, PhD, Director
sue.martin@med.usc.edu

Assistant: Gina Madrid
virginia.madrid@health.usc.edu
323-442-9622

Andy E. Sherrod, MD, Co-director
andy.sherrod@med.usc.edu

Assistant: Gina Madrid
virginia.madrid@health.usc.edu
323-442-9622

Mo-Li Chen, Supervisory Technologist
mhchen@usc.edu
323-865-3374

Alex Trana, Histotechnologist
trana@usc.edu
323-865-3374

5. CLINICAL TRIALS UNIT

- Overview of services provided

The Clinical Trials Unit (CTU) provides infrastructure, resources, and support to conduct human studies:

Infrastructure

- State-of-the-art space (outpatient and inpatient capabilities) for the conduct of early phase (drug development) and complex mechanistic trials
- Dexa scan, EKG, infusion equipment, serial pK and pD sample procurement and processing, bio-nutrition evaluations, and metabolic testing

Resources

- Research-trained staff, including research nurses, study coordinators, phlebotomists, radiology and laboratory technicians
- Specimen processing and handling laboratory on site with select and tailored

assay development and performance

Support

- Letter of support and preliminary budget for CTU-related services for grant applications
- Design and feasibility consultation meetings with CTU staff, clinical research expert(s), and biostatistics. The aim is to provide assistance with operational assessment and/or protocol development
- Data Safety and Monitoring Plan development assistance
- Networking opportunities
- Study coordinator, recruitment and data management services for junior investigators or investigators with limited departmental resources

• **How can researchers utilize the services provided?**

There are multiple ways to utilize the CTU. Researchers may complete the study conduct at CTU, including assistance with subject recruitment, eligibility work-up, study enrollment, serial visits, and completion of Case Report Forms. Alternatively, study participants may present to CTU on specific days for serial pK and pD sample procurement or serial safety evaluations. The CTU can also assist in the processing of bio-specimens obtained from research participants outside the CTU.

Investigators wishing to utilize the CTU are strongly encouraged to request a design and feasibility meeting by sending an email to ctu@sc-ctsi.org. Experts from pertinent areas – clinical operations, biostatistics, etc. – will help investigators develop research proposals, design a protocol, formulate a statistical plan, assess logistical and operational feasibility, and review resource utilization.

○ *What is the process in place to access the services?*

An online application must be completed to request services. An electronic consultation form is needed to assess and review CTU usage. Both documents are found on the CTU web page with specific links to each:

http://sc-ctsi.org/index.php/resources/conduct_human_studies_and_trials

○ *Who initiates the process?*

The investigator, or most often a designee (CRC, project specialist/manager, etc.), can complete the consultation and/or application online.

- *When should the process be started?*

The online application must be completed post-award and can be done in parallel to IRB submission. The electronic consultation form must be completed prior to acquiring funding.

- *Are there differences in the process between Keck Medical Center and LAC+USC?*

The services provided at the CTU remain the same but county (LAC+USC) personnel must obtain hospital (Keck Medical Center) credentials to conduct visits at the CTU in Norris Cancer Hospital. Your home department coordinator or administrator should be able to assist in acquiring the necessary forms. Otherwise, please contact the CTU and we will facilitate the process.

- **What are the charges involved?**

You may contact the CTU to discuss a specific study budget for your proposal and/or protocol.

- **List of contacts for the service/core**

The patient rooms are located on the 4th floor of the Norris Cancer Hospital.

Administrative offices:

USC Norris Cancer Hospital
1441 Eastlake Ave, Suite 1329
Los Angeles, CA 90033
Office: 323-865-3225
Fax: 323-865-0852
Email: ctu@sc-ctsi.org
Web: www.sc-ctsi.org/clinical

Anthony El-Khoueiry, MD, Director, Clinical Translation
elkhouei@med.usc.edu
323-865-3967

For all CTU-related questions, please contact

Julie Statzel, RN, CCRC, BSN, MHS
Deputy Director, SC CTSI CTU
Julie.Statzel@med.usc.edu; 323-865-3249

6. BIOSTATISTICS

USC investigators have multiple options for biostatistics help, depending on the nature of the support needed. The Norris Cancer Center Biostatistics Core focuses on **cancer studies**; the Statistical Consultation and Research Center focuses on **genetic-related research and clinical trials, as well as longer term statistical collaborations**; and the Southern California Clinical and Translational Science Institute's Biostatistics Program focuses on **short-term statistical collaborations** (e.g., assistance with study designs, analysis of existing data, etc.). Details about each option, as well as other opportunities for statistical consultation, are provided below.

Norris Cancer Center Biostatistics Core (Cancer Center members only)

- **Overview of services provided**

The Biostatistics Core provides statistical support to clinical, basic science, and cancer cause and prevention investigators. Statisticians bring to the Cancer Center expertise in the area of cancer clinical trials, epidemiologic research, and molecular epidemiology and genetics. This support may range from simple advice, to participating in the design of the research project, to carrying out aspects of the data management and statistical analysis of a project. The level of support depends on the scale of the project, the support staff available, and the expertise of the investigator. The statisticians in this Core work with members of the Clinical Investigations Support Office (CISO) and participate in the planning, monitoring, and analysis of in-house clinical trials approved by the Clinical Investigations Committee (CIC).

- **How can researchers utilize the services provided?**

Initial, short-term consultation is available to all Cancer Center members. For studies that involve more of a statistician's time, priority is given to Cancer Center projects that have received peer-reviewed funding or are part of the research effort of a funded Cancer Center investigator, studies that are deemed critical to a specific Cancer Center program, and to clinical studies that are rated outstanding by the CIC, that have received CISO support, or that are reviewed and approved by the Cancer Therapy Evaluation Program of the NCI.

Cancer Center investigators are strongly encouraged to request a design and feasibility meeting when developing research proposals; the statistical input would be integrated into that meeting. Topics in the meeting will include protocol design, statistical planning, feasibility analysis, resource utilization and funding strategies. Contact Zeno Ashai in CISO at (323) 865 0463 or Zeno.Ashai@med.usc.edu or [contact CISO](#) at

CoreCISO@med.usc.edu to schedule a meeting for you with representatives from all the relevant cores.

- **What are the charges involved?**

There is no charge to Cancer Center members for Biostatistics Core support.

- **List of contacts for the service/core**

USC Norris Comprehensive Cancer Center

[Biostatistics Core](#)

NOR 3419

1441 Eastlake Ave

Los Angeles, CA 90089

Dr. Susan Groshen, Director

groshen@usc.edu

323-865-0375

Dr. Richard Sposto, Co-Director

rsposto@chla.usc.edu

323-361-8582

(Researchers at Children's Hospital, may want to contact Dr. Richard Sposto or click [here](#) for Biostatistics Core contact information.)

Statistical Consultation and Research Center

- **Overview of services provided**

The Statistical Consultation and Research Center (SCRC) integrates statistical, epidemiological and computing resources and offers them to professionals conducting clinical and biomedical research. The SCRC consists of a team of statisticians, epidemiologists, programmers, project coordinators and data managers to support clinical and prevention trials, observational and retrospective studies, and cross-sectional and longitudinal surveys. Biostatistics and bioinformatics faculty and staff have particular expertise in statistical genetics, including study designs, developments of statistical methods, and analysis of genetic and other high-dimensional data.

- **How can researchers utilize the services provided?**

Any USC or non-USC investigator may request consultation; click [here](#) for contact information or by contacting Dr. Jim Gauderman (jimg@usc.edu).

- **What are the charges involved?**

All services are by recharge with the first hour free.

- **List of contacts for the service/core**

Click [here](#) for information on clinical Research Design

Click [here](#) for information on Statistical Consultation.

Click [here](#) for information on Methodological Research

David Conti, Associate Professor of Preventive Medicine
David.Conti@keck.usc.edu

Jim Gauderman, Professor of Preventive Medicine
jimg@usc.edu

Southern California Clinical and Translational Sciences Institute (SC CTSI) Biostatistics Program

- **Overview of services provided**

To support efficient and accurate data collection and analysis, and to help researchers avoid translational research pitfalls, the [SC CTSI](#) provides a variety of free consultation services, with an option to purchase additional services on a recharge basis. Statistics services include short- and long-term consultations on issues related to study design, including power and sample size estimation, randomization schemes, development of data acquisition and management plans, development of statistical analysis plans, statistical analysis of study data and analytic summaries.

- **How can researchers utilize the services provided?**

Consultation is available to all USC and non-USC investigators. Priority is given to: 1) NIH-funded, junior investigators; 2) those planning to apply for NIH-funding. Investigators using the Clinical Trials Unit (CTU) are strongly encouraged to request a design and feasibility meeting when developing research proposals; the statistical input

would be integrated into that meeting.

To submit a request for biostatistics consultation, go to:

http://sc-ctsi.org/index.php/resources/get_expert_advice

- **What are the charges involved?**

Initial consultations are free with an option to purchase additional services on a recharge basis.

- **Initial consultation (up to 1 hour):** Free for any project based at USC, CHLA and affiliated SC CTSI institutions
- **SC CTSI Pilot Funding Awardees:** Any SC CTSI Pilot Funding Awardee can receive up to 2 hours free for work related to the funded project
- **Junior Investigators:** Junior Investigators, as defined by NIH and/or in an Assistant professor classification, may receive up to 5 free hours of support
- **K awardees:** All K awardees may receive up to 15 hours free in total annually for their K – related project based at USC, CHLA and affiliated SC CTSI institutions
- **T scholars:** All T scholars may receive up to 15 hours free in total annually for their T – related project based at USC, CHLA and affiliated SC CTSI institutions
- **Extramural Grant Planning:** Researchers seeking support in the preparation of grants for submission within 6 months may receive up to 3 free hours of services in support of the grant application

Recharge rates: \$125/hour after initial consultation

- **List of contacts for the service/core**

SC CTSI Biostatistics Program

bbr@sc-ctsi.org

Other Opportunities:

1. USC Information Technology Services (ITS) Statistical Consulting offers short-term consulting services for use of statistics software for anyone in the USC community.

Contact:

ITS Statistical Consulting (stats@usc.edu) or

Brenda Osuna, Senior Statistics Consultant; brendao@usc.edu

2. Certain NIH-funded center grants include biostatistics service cores that usually are mandated to provide services to center members. Such centers include the Alzheimer Disease Research Center (Department of Neurology) and the Southern California Environmental Health Sciences Center (Division of Environmental Health, Department of Preventive Medicine).
3. A small number of departments fund some portion of a biostatistician to work with faculty and fellows. Check with your department chair or research administrator.

7. CARDIOLOGY

Echocardiography services are available at the CardioVascular Thoracic Institute (CVTI), Keck Hospital of USC, and LAC+USC Medical Center. There is also an Echo Core Lab that can accommodate more complex orders.

CVTI OR KECK HOSPITAL OF USC

- **Overview of services provided**

The CVTI can accommodate outpatient research echo requests. As part of each trial, the CTO will develop a standard research order form that includes an echocardiogram request; that form should be submitted to CVTI at the time of research echo request.

For inpatients, echocardiograms can be ordered through Cerner like a regular echocardiogram. In the comments section for the order, "research" should be input and which study so that techs know how to modify echo as needed. If the study would be done for clinical purposes and is not being done for research purposes only, the comment is not necessary.

If the study calls for a regular echo, then staff will do a regular echo. If more complex echos are needed, details will need to be provided in order to educate staff in advance.

- **How can researchers utilize the services provided?**

The PI or study team should contact one of the individuals listed below during the planning process in collaboration with IRB and CTO. The PI or study team will provide protocol, examination details and proposed CPT codes related to the type of echocardiogram needed to fulfill the study and budgetary requirements. The study team should ensure that CTO budgets adequately for the echocardiogram and develops an appropriate research order form.

- **What are the charges involved?**

Information on expenses can be accessed via the USC Clinical Trials Office.

- **List of contacts for the service/core**

Click [here](#) for additional CVTI staff and faculty contact information

Susana Perese, BS, RVT, APS, FASE, Director, Noninvasive CardioVascular
Diagnostic Services, Cardiac Cath Lab

susana.perese@med.usc.edu

323-442-6015 / fax 323-442-6005

Rafael Llerena MPH, RDMS, RDCS, FASE, Supervisor, Noninvasive Cardiology
Department

Rafael.Llerena@med.usc.edu

323-442-9947 / fax 323-442-8642

LAC+USC Medical Center

- **Overview of services provided**

The same process for incorporating research echocardiograms into the budget and research order forms applies to studies performed at LAC+USC Medical Center. The PI and study team should be aware that research echocardiograms that are budgeted appropriately can be performed at CVTI or Keck Hospital as long as a research order form is completed. If the echocardiograms have to be performed at LAC+USC Medical Center and will require a large number of studies on a regular basis, this would have to be discussed with Art Murga (Chief, Non-Invasive Services; Jimmie Smith [Administrator, Non-Invasive Services] to take over for him next year) and Danny Amaya (Administrator, Diagnostic Services) for approval.

If an inpatient echocardiogram is ordered for research purposes, it will usually be done like any other inpatient echocardiogram. If there is a specific time frame needed (like must be done within 24 hours), then a phone call should be made to the echo lab/echo fellow to make sure it gets done when needed. Similarly to outpatients, if any study going forward were to require a consistent or high number of echocardiograms, approval would be required for funding/extra time, etc.

- **List of contacts for the service/core**

Izabella Hassadourian ihassadourian@dhs.lacounty.gov; 323.409.7579

ECHO CORE LAB

- **Overview of services provided**

In addition to the standard echo orders and reads, another option for cardiology services is the Echo Core Lab, directed by Tracy Lawrence, MD. This would be a resource when researchers want echo reads that require measurements that are particularly complex and outside of the standard echo report. The echo core lab is experienced in reading echos for large multicenter trials to ensure standardization and quality of echo reads. They are available to serve as the echo core lab for USC investigator-initiated trials and industry sponsored trials.

- **How can researchers utilize the services provided?**

Investigators should contact Christine Tam for further information.

- **List of contacts for the service/core** or click [here](#) for additional contact information for USC Cardiovascular Medicine

Christine Tam
Clinical Project Manager
Cardiovascular Research Unit (CRU)
University of Southern California
Division of Cardiovascular Medicine
1510 San Pablo St, Suite 322
Los Angeles, CA 90033
Phone: 323-442-6863
Fax: 323-442-7610
Email: cru@med.usc.edu

8. OPHTHALMOLOGY

- **Overview of services provided**

The Ophthalmology Clinical Trials Unit provides comprehensive ophthalmic exams and diagnostics through a variety of subspecialty services in support of human studies.

Specialties

- Comprehensive Ophthalmology
- Cornea
- Retina
- Glaucoma
- Oculoplastics
- Neuro-Ophthalmology
- Ocular Oncology
- Uveitis

Exams

Ophthalmology services may include a focused, straightforward exam through a comprehensive high level exam.

A typical exam may include the following:

- Patient History
- Visual Acuity
- Depth Perception
- Color Recognition
- Muscle Movements
- Peripheral Vision
- Pupil Response
- Tonometry (Eye Pressure)
- External Examination (cornea, eyelids, conjunctiva)
- Retinal Dilated Examination (fundus, optic nerve, macula)

Diagnostics

Ophthalmic diagnostics are offered in a wide range of on-site services. These services include the following:

- Fundus Photography
- Fluorescein Angiography/Fundus Auto Fluorescence
- Optical Coherence Tomography
- Electrophysiology
- Ultrasound
- Pachymetry
- Specular Microscopy
- Gonioscopy

- Extended Ophthalmoscopy
- Visual Field
- Corneal Topography

- **How can researchers utilize the services provided?**

Ophthalmology service for clinical trials may be accessed through the following procedure:

1. The requesting department PI or Coordinator should initiate contact with the ophthalmology clinical trial unit.
2. The scope of the trial and needed services should be presented through a Research Order Form (ROF), schedule of visits, and instructional documentation related to the requested services.
3. Charges should be obtained through the ophthalmology charge master on file with the USC Clinical Trials Office.
4. A full review by the ophthalmology PI and ophthalmology clinical trial unit will be conducted with feedback on available resources and clinical registration procedures.

- **What are the charges involved?**

Refer to the charge master on file with the USC Clinical Trials Office.

- **List of contacts for the service/core**

Click [here](#) for contact information for the Department of Ophthalmology.

Ophthalmology Clinical Trials Unit
1450 San Pablo Street, 4th Floor
Los Angeles, CA 90033
323-442-6335 / fax 323-442-6496

Raya Karelin, Senior Clinical Administrative Director I
rkarelin@usc.edu

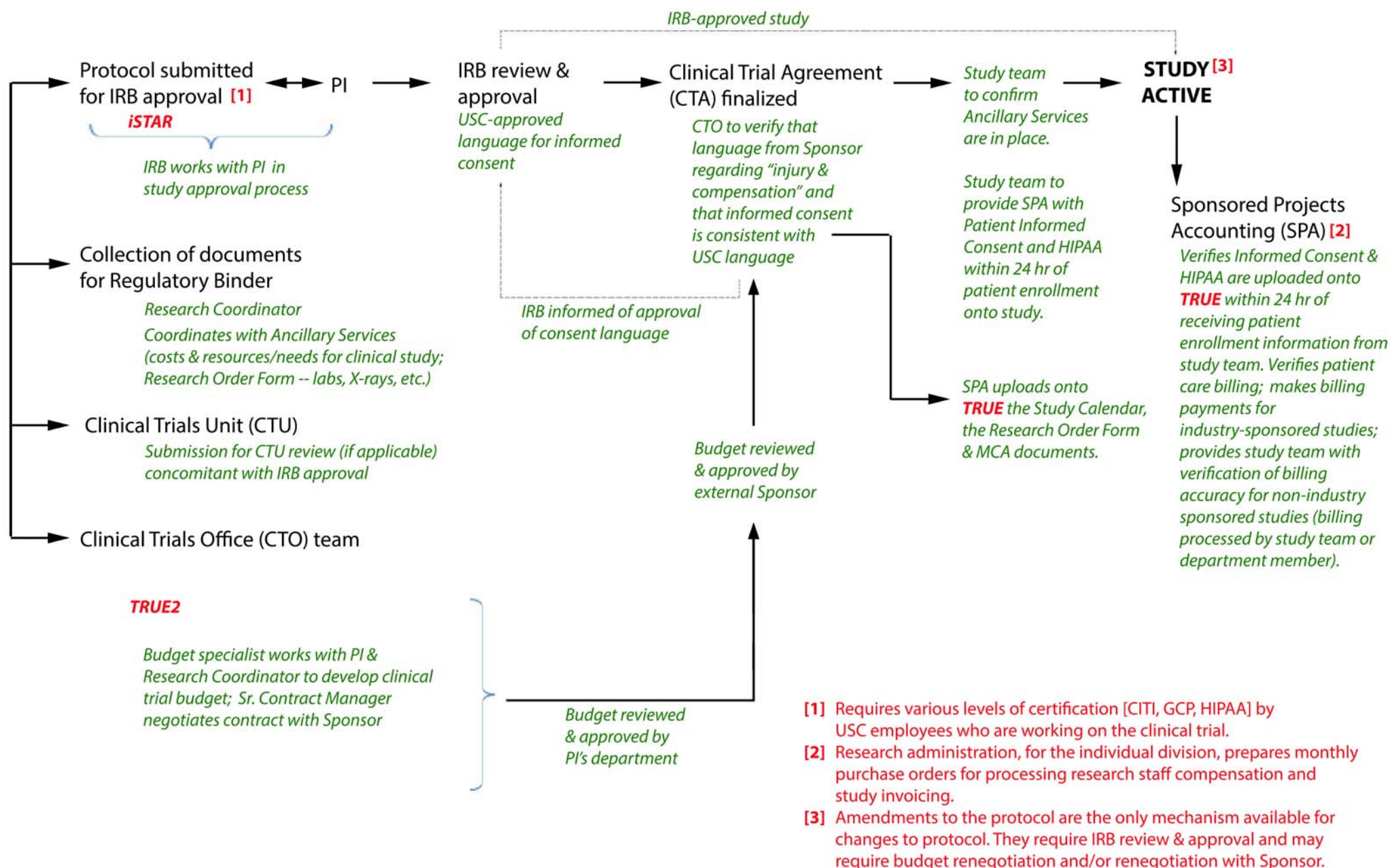
9. PRIMARY CONTACTS FOR ACCESSING ANCILLARY SERVICES OR SUPPORT

Service/Support	Primary Contact	Email/Phone
Biostatistics		
Norris Cancer Center Biostatistics Core	Susan Groshen or Richard Sposto (CHLA)	groshen@usc.edu 323-865-0375 rsposto@chla.usc.edu 323-361-8582
Cancer Epidemiology Program	Jim Gauderman	jimg@usc.edu 323-442-1567
SC CTSI Biostatistics Program	bbr@sc-ctsi.org	bbr@sc-ctsi.org
ITS Statistical Consulting	Brenda Osuna	brendao@usc.edu
Cardiology		
Keck Hospital of USC or CardioVascular Thoracic Institute	Susana Perese or Rafael Llerena	susana.perese@med.usc.edu 323-442-6015 Rafael.Llerena@med.usc.edu 323-442-9947
LAC+USC Medical Center -	Izabella Hassadourian	ihassadourian@dhs.lacounty.gov 323.409.7579
Echo Lab	Christine Tam	cru@med.usc.edu 323-442-6863
CTU		
General	Julie Statzel	Julie.Statzel@med.usc.edu 323-865-3249
Operations	Yolanda Stewart	cerda@usc.edu 323-865-3056
Nursing	Aura Marroquin	marroqui@usc.edu 323-865-0641
Laboratory	Lilit Baronikian	yegiyant@usc.edu 323-865-3379
Billing	Rachel Spencer	spencer1@usc.edu 323-865-3087
Scheduling	Michelle Munevar	ctusched@usc.edu or

		ctucancellation@med.usc.edu 323-865-0345
Molecular Imaging Center	Madlen Aladadyan	maladady@usc.edu 323-442-3858
Ophthalmology	Raya Karelin	rkarelin@usc.edu (323) 442-6576
Pathology		
Study Planning	Sue Ellen Martin (asst. Gina Madrid) or Andy E. Sherrod (asst. Gina Madrid)	sue.martin@med.usc.edu 323-442-9622 andy.sherrod@med.usc.edu 323-442-9622
Implementation	Mo-Li Chen or Alex Trana	mhchen@usc.edu 323-865-3374 trana@usc.edu 323-865-3374
Pharmacy		
Norris Cancer Center or CTU	Caroline Chellamy	IDSParmacy@med.usc.edu 323-865-3538
LAC+USC Hospital or other clinic/site	Caroline Chellamy	IDSParmacy@med.usc.edu 323-865-3538
Keck Hospital of USC	Caroline Chellamy	IDSParmacy@med.usc.edu 323-865-3538
Radiology	Bhushan Desai and Sam Valencerina (special imaging)	bhushand@usc.edu 323-865-9949 Samuel.valencerina@med.usc.edu

APPENDIX 1 - INDUSTRY-SPONSORED CLINICAL TRIALS AT USC (SPONSOR & PI-INITIATED)

All cancer-related study protocols must first be submitted for review/approval by the Clinical Investigations Support Office (CISO). Confidentiality Agreements (if applicable) must also be signed and approved prior to submission of study to iSTAR

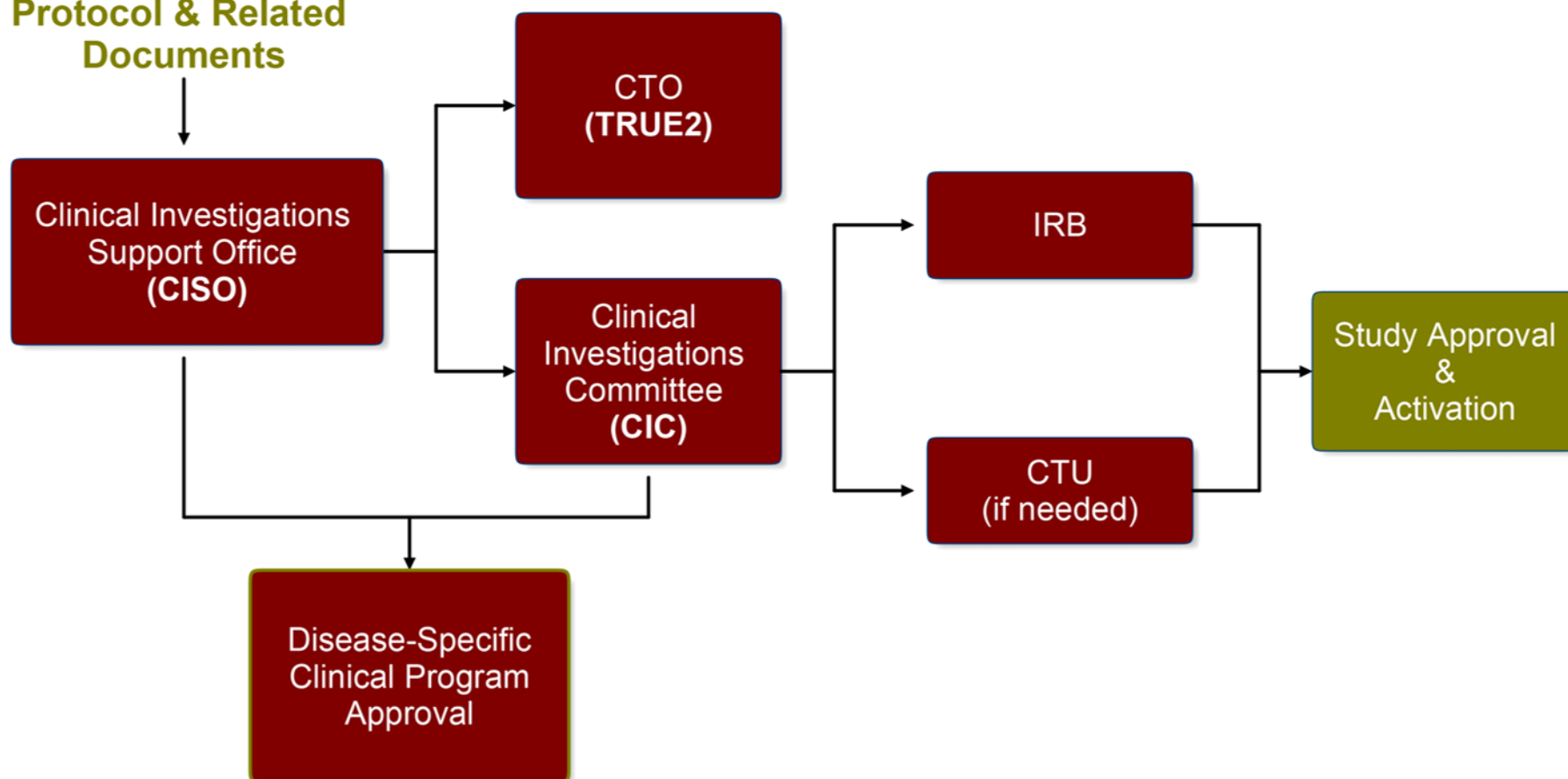


Appendix 2. Cancer-Related Clinical Trials at USC

All clinical and translational protocols at USC that involve human subjects and are designed to address a cancer-focused scientific question must be reviewed and approved by CIC prior to IRB review and approval.

The cancer-focused scientific question may be related to cancer diagnosis, screening, prevention, or treatment.

Single Point of Entry
Protocol & Related
Documents



CISO serves as the single point of entry for all cancer related protocols and centrally manages the process of study review and activation

APPENDIX 3. CLINICAL RESEARCH ROLES

This appendix provides a brief description of the roles of key persons at USC associated with **Human Subject Research (HSR)**, which includes:

- Clinical trials;
- Research using human biological materials;
- Retrospective research involving record reviews;
- Focus group testing or survey research;
- Studies that have IRB approval from other organizations, including approval from other government entities;
- Off-site studies, domestic or foreign, including studies with other government agencies or academic institutions;
- Studies associated with the Food and Drug Administration (FDA), including the FDA's private database information, either alone or in collaboration with another government agency.

CLINICAL STUDY TEAM

Principal Investigator (PI): The PI is responsible and accountable for the preparation, integrity of the design, conduct, and management of the clinical study, assuming full responsibility for the treatment, safety and evaluation of human subjects, and for the integrity of the research data and results. The PI may delegate responsibility to individual members of the research team; however, the PI cannot delegate accountability for the ethical conduct of the study. The PI is also responsible for the direction and oversight of compliance, personnel and collaborators, financial and budgetary management, and for coordination with school, department, and central administration personnel to assure research is conducted in accordance with local, state and federal regulations, as well as USC and sponsoring agency policies and procedures. In clinical trials that are investigator initiated, the PI also assumes the responsibilities of the Sponsor. In addition, the PI is responsible for:

- Ensuring the disclosure of financial interest and arrangements of any member of the research team that may present a conflict of interest to the sponsor, IRB and/or to the study participants.
- Ensuring IRB approval for the study is obtained before any subjects are enrolled.
- Ensuring informed consent is obtained in accordance with FDA regulations.
- Administering the drug or using the device only in subjects under the investigator's supervision or under the supervision of a recognized sub-investigator.

- Maintaining adequate records of the dispensation of the drug or device.
- Returning unused materials at the end of trial, if applicable.
- Preparing and maintaining adequate case histories documents.
- Maintaining correspondence with the IRB and the sponsor to ensure that both have reviewed protocol amendments, recruitment materials, and the Investigator Brochures (IB) and notifying the sponsor if IRB approval is withdrawn.
- Providing progress, safety, and final reports.

Co-Principal Investigator (Co-PI): Co-PIs are key personnel who have responsibilities similar to those of a PI on human studies research projects. While the PI has ultimate responsibility for the conduct of a research project, the co-PI is also obligated to ensure the project is conducted in compliance with applicable laws and regulations and institutional policy governing the conduct of research on human subjects.

Research Coordinator: Works under the direction of the PI to support, facilitate and coordinate the daily activities of the clinical study. Responsibilities include: supports the safety of clinical research patients/participants; coordinates protocol-related research procedures (e.g., collection of documents for Regulatory Binder), study visits and follow-up care; screens recruits and enrolls patients/research participants; maintains study source documents; reports “Reportable Events” (e.g. adverse events); understands Good Clinical Practice (GCP) and regulatory compliance; educates subjects/research participants and family on protocol, study intervention, study drugs, etc.; complies with institutional policies, standard operating procedures and guidelines; and complies with federal, state and sponsor policies. For studies performed outside of the Clinical Investigations Support Office (CISO), responsibilities of the Research Coordinator also include those of the Regulatory Manager, the Data Manager, as well as submission to, and negotiation with the USC Clinical Trials Office.

Study Monitor: The study monitor is responsible for monitoring the clinical study and reports to the study Sponsor. Monitor responsibilities include: performing site visits, and ensuring that adequate and accurate records are kept; all reportable events are recorded; study drugs are accounted for; the study protocol is being followed; informed consent is obtained, and the rate of patient enrollment is meeting established targets, among others. The frequency of site visits and complexity of the monitoring plan depends on a number of factors, such as the complexity of the protocol, the disease being evaluated, the level of experience of the investigator/staff, site performance history.

Data Manager: The Data Manager is responsible for set-up and maintenance of the clinical study database, data entry, as well as statistical analysis of study data.

Sponsor: A sponsor may be an individual, a private company, an institution or other organization that is responsible for the initiation of a study involving a drug, device, or biologic. The sponsor is always the entity that funds the clinical research.

Post-Doctoral Scholar: A Postdoctoral Scholar at USC may qualify as a co-PI but may not be the principal investigator of a clinical trial, unless a specific waiver and approval is granted by the Office of Research and upon recommendation by the Department and approval of the appropriate Dean. Postdoctoral scholars must qualify as a Postdoctoral Research Associate; Postdoctoral Fellow or Postdoctoral Teaching Fellow. The Postdoctoral Research Associate or Postdoctoral Teaching Fellow is appointed as a temporary, fixed-term employee of the University. The Postdoctoral Fellow is registered as a non-matriculated, non-degree seeking, and limited status student of the University. Postdoctoral Scholars must have been awarded a Ph.D. or equivalent doctorate in an appropriate field within five years of initial appointment.

CLINICAL TRIALS OFFICE (CTO)

Clinical Trial Financial Administrator: The Clinical Trial Financial Administrator is responsible for conducting the Medicare Coverage Analysis (MCA). Through this process the Financial Administrator identifies and differentiates between costs that are study related and should be charged to the study sponsor and those costs that are routine patient care that would occur independent from the study and therefore could be charged to Medicare or third party insurance.

Budget Specialist: The Budget Specialist is responsible for developing and negotiating clinical trial budgets. The Budget Specialist starts working on developing the budget after receiving the Medicare Coverage analysis (MCA) and in collaboration with the Principal Investigator and other administrative participants.

Senior Contract Manager: The Senior Contract Manager is responsible for reviewing, negotiating, and executing the Clinical Trial Agreement (CTA).

CLINICAL INVESTIGATIONS SUPPORT OFFICE (CISO), NORRIS COMPREHENSIVE CANCER CENTER (NCCC)

Regulatory Manager: The Regulatory Manager ensures that the clinical study meets compliance requirements of all local, state and federal regulations, as well as USC and sponsoring agency policies and procedures. Responsibilities include preparing and/or overseeing the preparation of regulatory submissions, including safety reports, amendments, supplements and license renewals, original applications to the FDA (i.e.: Investigational New Drug (IND), Clinical Trial Applications (CTA), New Drug Applications (NDA), Marketing Authorization Applications (MAA), and Biologics License Applications (BLA)). Additional responsibilities may include providing regulatory review of clinical protocols and development documents, ensuring IND/NDA information is updated and maintained in accordance with requirements, and providing strategic regulatory advice to assigned project teams in coordination with Regulatory Affairs management

Clinical research staff may fall in one of these positions, depending on their job responsibilities:

RN RCs:

Research Nurse (#185607): Functions as a team member in the recruitment, assessment, treatment, data collection and follow-up for patients enrolled in a research study.

Research Nurse Senior (#- 185611): Functions as a team member in the recruitment, assessment, treatment, data collection and follow-up for patients enrolled in a research study.

Protocol Coordinator (Research Nurse, #185615): Assists principal investigator in coordinating all phases of research studies including recruitment, assessment, treatment, data collection and follow-up for enrolled patients. Provides input to principal investigators, staff nurses and patients that effects clinical research studies from the initial protocol design to completion of study.

Sr. Protocol Coordinator (Research Nurse, #185619): Serves as a team leader in the recruitment, assessment, treatment, data collection and follow-up for patients enrolled in a research study. Provides leadership and direction for daily research study operations and administrative activities. Assists principal investigator in coordinating all phases of research studies. Provides input to principal investigators, staff nurses and patients that effects clinical research studies from the initial protocol design to completion of study and final publication.

Non-RN RCs:

Research Coordinator I: Assists investigators or other staff with research studies in subject recruitment, data collection, scheduling of study-related activities and follow-up of enrolled subjects.-

Research Coordinator II: Serves as a lead coordinating aspects of sponsor-initiated and investigator-initiated research studies including subject recruitment, data collection, scheduling of study-related activities and follow-up of enrolled subjects. Assists with budget preparation and training of less experienced research coordinators. Provides guidance and direction related to research studies to investigators, research personnel, and subjects, from initial protocol design to completion of study and close-out report.

Research Coordinator Supervisor: Supervises and coordinates all aspects of sponsor-initiated and investigator-initiated research studies including subject recruitment, data collection, scheduling of study-related assessments and follow-up of enrolled subjects, budget development and administration. Supervises staff and plans project operations based on proposed research activities and timelines. Provides leadership, guidance and direction related to research studies to investigators, research personnel and subjects, from initial protocol design to completion of study and close-out report.

Clinical Research Data Specialist: Lead Coordinates, facilitates and manages the clinical data for various phases of complex clinical trials. Assists Study Coordinators and Clinical Research Data Specialist II with complex clinical trials. Provides leadership, guidance and direction to Clinical Research Data Specialists.

OFFICE OF COMPLIANCE

Director of Research Compliance: The Director of Compliance is responsible for performing periodic risk assessments; conducting periodic monitoring and auditing; investigating allegations of non-compliance and recommending corrective action where appropriate.

Research Compliance Manager: The Research manager is responsible for providing training and education on ethical standards, policies, and procedures and assisting in the development of standards, policies, and procedures to prevent and detect violations

SPECIAL PROJECTS ACCOUNTING (SPA)

Manager, SPA Special Projects Accounting: The SPA Manager is responsible for uploading the Study Calendar, Research Order Form and MCA on to TRUE. Responsibilities also include verifying that Informed Consent and HIPPA documents are uploaded onto TRUE within 24 hours of receiving patient enrollment information from study team, as well as verifying participant care billing (i.e.: ensure billing is made to the appropriate entities – Medicare, sponsor or patient insurance, etc. – and that charges are billed at Medicare rates). For industry-sponsored studies, the office maintains study accounts and processes/pays study-related bills; for non-industry-sponsored studies, responsibilities are limited to verifying patient bills (actual invoicing is done by the appropriate study team member).

OFFICE FOR THE PROTECTION OF RESEARCH SUBJECTS (OPRS)

OPRS Executive Director: The Executive Director is responsible for establishing Human Subject Protection Program policies for USC as well as identifying and implementing best practices to ensure continued USC accreditation. Additional responsibilities include oversight of USC IRBs as well as the development of educational resources associated with human subjects research.

IRB Member: There are four Institutional Review Boards at the University of Southern California (one on the University Park Campus, and three on the Health Sciences Campus). IRB members review and approve human subject research to ensure it is in accordance with Department of Health and Human Services (DHHS), the FDA, and federal and state laws, as applicable. USC IRBs have the authority to approve, disapprove, or suspend human subject research projects, as well as observe, or have a third party observe the consent process and the conduct of the research. No USC faculty, staff, or student may conduct human subjects research without obtaining approval from the appropriate IRBs at either the Health Sciences or University Park Campuses.

APPENDIX 4. RESEARCH FACILITIES & CORE LABORATORIES

Resource Name	Campus	Contact	Contact Email	Contact Phone	Affiliation
Alfred E. Mann Institute for Biomedical Engineering	UPC		information@aminet.usc.edu	213-821-1745	
Biomimetic Microelectronics Systems Engineering Research Center	HSC		http://bmes-erc.usc.edu/about/contact.htm	323-442-6786	Keck and Viterbi
Bioreagent and Cell Culture Core	HSC	Nily Harel	CoreCellCulture@med.usc.edu	323-224-7792	Keck - NCCC
Biosafety Level 3 Research Laboratory		Jill Henley	jhenley@usc.edu	323-442-4833	Keck School of Medicine
Biostatistics Core	HSC/CHLA	Melanie Funes	bbr@sc-ctsi.org	(323) 442 1251	SC CTSI
Biostatistics Core Services	HSC	Susan Groshen	groshen@usc.edu	323-865-0375	Keck - NCCC
Cancer Research Informatics Core	HSC	Reed Comire	comire@usc.edu	323-442-7717	Keck - NCCC
Cell and Tissue Imaging Core	HSC	Ernesto Barron	coreconfocal@med.usc.edu	323-442-6622	Keck - NCCC
Center for Electron Microscopy and Microanalysis	UPC	John Curulli	curulli@usc.edu	213-740-1990	Dornsife College & Viterbi
Center for Liver Disease (Cell Culture)	HSC	Maggie Castillon	margarsc@usc.edu	323-442-1800	Keck
Center for Quantum Information Science & Technology (CQIST)	UPC	Daniel Lidar	lidar@usc.edu	(213) 740-0198	Viterbi & Dornsife
Chemistry Instrumentation Facility	UPC	Michele Dea	michele@usc.edu	213-740-7036	Dornsife
Circulating Tumor Cell Research Core	HSC	Amir Goldkorn	agoldkor@usc.edu	N/A	Keck - NCCC
Cognitive Neuroscience Imaging Center	UPC	JC Zhuang	jc.zhuang@gmail.com	213-821-2199	Dornsife Cognitive Neuroscience Imaging Center
CTSI-Southern California Clinical and Translational Science Institute	HSC	General Inquiries	info@sc-ctsi.org	323-442-4032	CTSI
Department of Animal Resources	HSC	General Inquiries	daradm@usc.edu	323-442-1689	Department of Animal Resources
Diabetes and Obesity Research Institute (DORI) Clinical Services Core	HSC	Christina Ayala	trujillc@usc.edu	323-442-2500	
Diabetes and Obesity Research Institute (DORI) Metabolic Assay Core	HSC	Christina Ayala	uscdori@usc.edu	323-442-2500	Keck
Epigenome Center	HSC	Kendra Bergen	kendra.bergen@usc.edu	323-442-7951	Keck - NCCC
Flow Cytometry Core	HSC	Lora Barsky	facscore@gmail.com	323-442-7942	Broad Center

GUIDE TO CLINICAL RESEARCH AT USC

Resource Name	Campus	Contact	Contact Email	Contact Phone	Affiliation
Geographic Information Systems Laboratory	UPC	Leilani Banks	spatialsciences@dornsife.usc.edu	213-740-5910	Dornsife
Histology Laboratory	HSC	Jennica Zaro Liana Asatryan	zaro@usc.edu asatryan@usc.edu	323-442-1933	School of Pharmacy
IGM (Glasswash)	HSC	Elsie Ang	igm@usc.edu	323-442-1148	Keck
Image Processing and Informatics Lab	UPC	Brent Liu	ipilab2013@gmail.com	323-442-7050	Keck
Immune Monitoring Core	HSC	Diane Da Silva	diane.dasilva@med.usc.edu	323-442-3869	Keck - NCCC
Information Technology Services	UPC	Various (see web site)	Various (see web site)	213-740-2840	Information Technology Services
Lentiviral Core Laboratory	HSC	Liana Asatryan	asatryan@usc.edu	323-442-1427	School of Pharmacy
Machine Shop Facilities	UPC	Don Wiggins	dwiggins@usc.edu	213-740-6111	Viterbi
Molecular and Cell Biology (MCB) Support Core	HSC	Kent Chang	Coresharedequip@med.usc.edu	323-442-7725	Keck - NCCC
Molecular Genomics / DNA Oligo and Sequencing	HSC	Various (see web site)	Various (see web site)	323-442-7813	Keck - NCCC
Molecular Genomics / Genomics	HSC	Kendra Bergen	coregenomics@med.usc.edu	323-442-7813	Keck - NCCC
Molecular Genomics / Methylation	HSC	Kendra Bergen	coregenomics@med.usc.edu	323-442-7786	Keck - NCCC
Molecular Imaging Center - Small Animal Imaging	UPC	Grant Dagliyan	miclab@usc.edu	323-442-1166	Keck
Multi-Photon Microscopy Core	HSC	Dr. Janos Peti-Peterdi	petipete@usc.edu	323-442-4337	Keck - Zilkha Neurogenic Institute
Nanobiophysics Core	UPC	Shuxing Li	shuxingl@usc.edu	213-740-8491	Dornsife
NCCC Bioinformatics Core	HSC	General Inquiries	vasu.punj@usc.edu	323-442-7510	Keck - NCCC
Neuroplasticity and Imaging	HSC	Beth Fisher	bfisher@usc.edu	323-442-2796	Ostrow, Division of Biokinesiology and Physical Therapy
Non-Parenchymal Liver Cell Core & Animal Core	HSC	Hide Tsukamoto	htsukamo@usc.edu	323-442-3121	Keck
Norris Library Bioinformatics Support	HSC	Yibu Chen	nmlbio@usc.edu	323-442-3309	Norris Library
PharmacoAnalytical Core	HSC	Al Barrientos	abarrien@usc.edu	323-442-1357	Keck - NCCC
Photonics Center	UPC	Donghai Zhu	donghaiz@usc.edu	213-740-1065	Viterbi
Proteomics Core Facility	HSC	Ebrahim Zandi	zandi@usc.edu	323-865-0644	Keck - NCCC
Reproductive, Endocrinology & Infertility Research Lab	HSC	Diane Quan	dianequa@usc.edu	323-226-3026	Keck

GUIDE TO CLINICAL RESEARCH AT USC

Resource Name	Campus	Contact	Contact Email	Contact Phone	Affiliation
Statistics Consultation & Research Center	HSC	W. James Gauderman	mtrujill@usc.edu	323-442-1810	Keck
Stem Cell Core	HSC	Victoria Fox	stemcellcore@med.usc.edu	323-442-7834	Broad Center
The Choi Family Therapeutic Screening Facility	HSC	Justin Ichida	ichida@usc.edu	323-442-8089	USC Stem Cell
Transgenic/ Knockout Rodent Core Facility	HSC	Nancy Wu	nwu@usc.edu	323-865-0726	Keck - NCCC
Translational Imaging Center	UPC	Cosimo Arnesano	arnesano@usc.edu	213-740-2233	Dornsife
Translational Pathology Facility - Slides & Soft Tissue	HSC	Sue Ellen Martin	CoreTransPath@med.usc.edu	323-442-9759	Keck - NCCC
Translational Research Laboratory	HSC	Jennica Zaro	zaro@usc.edu	323-442-1933	School of Pharmacy
UPC Genome & Cytometry Core	UPC	Daniel Campo	dcampo@usc.edu	TBD	USC Resource
USC Center of Excellence for Molecular Characterization	UPC	Allan Kershaw	kershaw@usc.edu	213-740-6376	Dornsife
USC Digital Repository	UPC	Linda Truong	Intruong@usc.edu	213.740.9263	USC Resource
USC Energy Institute	UPC		http://energy.usc.edu/contact/	(213) 740-1076	
USC Imaging Core	HSC	Seth Ruffins	ruffins@usc.edu	323-442-8083	Broad Center
Video Tracking Core	UPC	John Tower	jtower@usc.edu	213-740-5384	
West Semitic Research Project	UPC	Bruce Zuckerman	mlundber@usc.edu	213-740-3405	USC Resource
X-Ray Crystallography Facility	UPC	Ralf Haiges	haiges@usc.edu	213-740-3197	Dornsife

APPENDIX 5. CTO SCOPE OF SERVICES

The Clinical Trials Office (CTO) facilitates clinical research by providing the USC researcher community with comprehensive administrative services that help move trials quickly from initial concept to study completion.

The CTO provides budget development, Medicare Coverage Analysis (MCA), contract negotiation and execution for industry-sponsored clinical trials, in addition to performing the MCA for non-industry sponsored clinical trials. The CTO, through Sponsored Projects Accounting (SPA), also invoices sponsors for clinical research costs and reimburses providers (e.g., Keck Medical Center, research pharmacy, clinical trials unit) for costs of services and goods used in the research.

INDIRECT COST RATES AND CONTRACT SERVICES BY SPONSOR AND AGREEMENT TYPE

Industry-Sponsored Clinical Trials (Sponsor or PI initiated)

The CTO provides budget development, coverage analysis and contract negotiation and execution for both Sponsor and Principal Investigator (PI) Initiated clinical trials funded by industry.

Industry-sponsored clinical trials are any research activity that involves a drug, device, or biologic, (test article) subject to prior submission to the FDA as part of an application for a research or marketing permit or is not subject to prior submission but is intended to be submitted later as part of an application for a research or marketing permit. Clinical trials are designed to determine efficacy and safety of the test article.

Industry-sponsored clinical trials are assessed the Industry Clinical Trial indirect cost rate of 35% of Total Direct Cost (excluding certain fees).

INDUSTRY SPONSORED DRUG OR DEVICE AGREEMENTS

These are instances where a sponsor provides a drug or device for a clinical trial, without funding from the sponsor. The agreement providing the drug or device will often have the same terms and conditions as sponsor-initiated clinical trial agreements (CTA).

The source of funding must be identified by the PI, department and/or School and the CTO will work with them to ensure resources are sufficient to conduct the trial, and to ensure

compliance with regulations related to use of federal funds or other restricted funds.

NON-INDUSTRY SPONSORED CLINICAL RESEARCH PROJECTS WITH PATIENT CARE

Non-industry sponsored clinical research projects are negotiated and executed by the Department of Contracts and Grants (DCG), Health Sciences Campus.

Currently, every clinical project, regardless of sponsor, involving patient care must be submitted to CTO for a Medical Coverage Analysis (MCA; see below). Once the MCA is completed, costs for clinical procedures and labs chargeable to award/sponsor are identified and attached to the completed MCA. CTO also conducts a consistency review with the approved Informed Consent Form (ICF) from the IRB to make sure that terms included in ICF with respect to payments and subject injury are consistent with the grant or contract terms accepted by the University.

For all non-industry sponsors, clinical trials are assessed the Federal Research indirect cost rate, which is currently 64% of Modified Total Direct Costs (MTDC). MTDC exclude patient care costs, equipment >\$5,000 and some other specific items.

CONFIDENTIALITY DISCLOSURE AGREEMENTS (CDA)/NON-DISCLOSURE AGREEMENTS (NDA) FOR INDUSTRY-SPONSORED CLINICAL TRIALS

Clinical trial sponsors may require that the PI and/or study staff sign a Confidential Disclosure Agreement (CDA) or Non-Disclosure Agreement (NDA) before reviewing confidential documents, such as the Investigator Brochure, Protocol, and other non-public or proprietary information, to evaluate USC's interest in conducting the clinical trial. CDAs and NDAs assure that the sponsor that the institution will protect the confidential information against unauthorized disclosure for a period of time. The PI may acknowledge her or his responsibilities under the CDA, but only the CTO can execute the CDA on behalf of the University.

BUDGET DEVELOPMENT AND NEGOTIATION

The CTO provides budget development and negotiation services for clinical trials funded by industry. For non-industry funded trials, budgets are developed within the administrative unit (division, department) of the PI. CTO Budgeting can provide assistance in identifying rates and costs for clinical services. Negotiation services are provided by the Department of Contracts and Grants, Health Sciences Campus.

A successful clinical trial will include a budget that adequately meets the financial needs for all research activities required to conduct the clinical trial. The CTO will work with the PI or

Research Coordinator to ensure that the amount agreed upon by the Sponsor will adequately cover all costs associated with conducting a clinical trial. All final budgets will be approved and signed by the PI and Department Chair/Center Director, or designee.

For internally sponsored clinical research and trials, CTO conducts a MCA to identify study costs that fall under routine patient care costs, which would be chargeable to third party insurance or Medicare. All other costs must be borne by the project. The PI must provide an unrestricted account with sufficient balance to cover those costs that are not categorized as routine patient care. All final budgets will be approved and signed by the PI and Department Chair/Center Director, or designee.

MEDICARE COVERAGE ANALYSIS

The CTO provides the MCA for clinical trials funded by both industry and non-industry sponsors, as well as internally sponsored clinical studies and trials.

An MCA determines whether a clinical trial meets the requirements for reimbursement by Medicare or other insurers for routine care costs. The MCA also determines a priori which items or services will be charged to a third party and which items will be charged to the research study. MCAs are required for all clinical research studies in which some items or services will be billed to a third party as part of standard medical care, whether the third party is Medicare or another provider. The MCA must be completed for such studies prior to contracting and prior to enrollment of study participants. Diagnostic or therapeutic patient care costs of a clinical trial include:

- Items or services that are typically provided absent a clinical trial (e.g., conventional care)
- Items or services required solely for the provision of the investigational item or service (e.g., administration of a non-approved chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
- Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service – in particular, for the diagnosis or treatment of complications.

Clinical studies and trials in which all charges are billed to the research project do not require an MCA. In such cases, all charges will be billed to the research project and none can be billed to third party payers.

POST AWARD BILLING

The CTO, through SPA, provides account receivable management for clinical trials funded by

industry. The CTO will collect based on the services rendered.

Post-award key functions provided by CTO include:

- Review the budget and payment terms and perform new account setup in Kuali system
- Create patient tracking logs
- Prepare, review, and submit invoices to sponsor as required by sponsor terms and conditions
- Review and monitor cash receipt vs. amount owed from sponsor
- Reconcile payments received from sponsor to study budget
- Perform administrative aspects of transferring and closing out funds at project completion
- Internal billing and payment for items and services used in the study as follows:
 - Costs authorized and approved as part of trial or study processed against awards created in USC's Kuali Financial System
 - Medical billings screened against approved budget, Research Order Form, current Informed Consent Form, and participant on and off study date
 - Monthly billings (i.e. pharmacy and CTU) screened against participant on and off study date
 - Charges allocated to third party or to study based on approved MCA
 - Work with the PI or Department Administrator to monitor that no incorrect or duplicate payments are made to the Hospital
 - Charges billed to study in accordance with the ROF, MCA and study budget and credited to the provider of the item or service using internal funds transfer
 - Dispute charges in cooperation with the PI and Department

APPENDIX 6 - DEFINITIONS

Adverse event: an unfavorable change in health or side effect that occurs in a **subject** in a **clinical trial** while receiving the study's treatment, or within a specified period of time after the treatment has been completed. Adverse events must be reported to the **IRB**, and serious adverse events (e.g., death, illness requiring hospitalization, life-threatening events, or events involving cancer or fetal exposure) must be reported to regulatory agencies.

Alternative dispute resolution: methods for settling disputes outside of court, such as through mediation or arbitration.

Association for the Accreditation of Human Research Protection Programs (AAHRPP): an organization that provides accreditation for human research protection programs (HRPPs). Accreditation means that a HRPP safeguards research participants beyond that which is required by federal law, that the HRPPs data are reliable and credible, and that the HRPP operates efficiently. In order to be accredited, a HRPP must follow certain rules of AAHRPP, including rules regarding **adverse event** reporting that exceed **FDA** requirements.

Bayh-Dole Act: U.S. federal law that permits U.S. universities, small businesses and non-profits to elect to pursue ownership of an invention resulting from federal government-funded research. Refer to 35 U.S.C. § 200-212.

Biological: a preparation, such as a **drug**, vaccine, or antitoxin, synthesized from living organisms or their products and used as a diagnostic, preventive, or therapeutic agent.

Budget (internal): Identifies research costs billable to the sponsor of a clinical trial and determines how funds are to be spent by the University.

Budget (sponsor): Specifies how money is to be paid to the University. The **sponsor** budget specifies costs likely to be incurred in a **clinical trial** and must be submitted before the clinical trial may begin. The sponsor budget must include both direct and **indirect costs** of the trial, and shall include applicable (non-refundable) start-up costs, per-visit patient costs, fixed costs and variable or pass-through costs, fees (e.g., **IRB** fees and facility fees), and Medicare coverage analysis.

California Public Records Act (CPRA): California law requiring inspection and disclosure of governmental records to the public upon request, unless exempted by law. Refer to Cal. Gov. Code § 6250 *et seq.*

Case report form (CRF): a compiled record of the data and other information on each **subject** in a **clinical trial** as required by the **protocol**. The data may be recorded on any medium, including magnetic and optical carriers, provided that there is assurance of accurate input and presentation, and can be verified.

Clinical Investigation: The FDA defines Clinical Investigation as any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not

include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies (CFR - Code of Federal Regulations Title 21).

Clinical Research: The NIH defines human clinical research as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies. (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research.

Clinical Trial: The NIH defines a clinical trial as a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective. Behavioral human subject research involving an intervention to modify behavior (diet, physical activity, cognitive therapy, etc.) fits this definition of a clinical trial. Human subject research to develop or evaluate clinical laboratory tests (e.g. imaging or molecular diagnostic tests) might be considered to be a clinical trial if the test will be used for medical decision making for the subject or the test itself imposes more than minimal risk for subjects.

Compassionate use: Use of an *investigational drug, device or biological* where no other available treatments are satisfactory; prior *IRB* approval is required. Compassionate use is used in situations such as where the *subject* does not meet *clinical trial* enrollment criteria or where trial has ended but subjects want to continue to receive treatment).

Conception: the formation of a definite and permanent idea of the complete and operative invention as it is to be applied in practice. In order to be *patentable*, an invention must be conceived and *reduced to practice*.

Confidential Disclosure Agreement (CDA; also referred to as a non-disclosure agreement (NDA)): an agreement entered into between the University and a *sponsor* to protect the confidentiality of a sponsor's *protocol*. A CDA is entered into before a sponsor provides its protocol to an *investigator*, who may be interested in conducting the associated *clinical trial*.

Confidentiality of Medical Information Act (CMIA): A California law that protects the disclosure of a patient's "medical information" by a health care provider or health care service plan without the patient's authorization. "Medical information" is any information regarding a person's mental or physical condition, or treatment, which includes or contains any element of personal identifying information sufficient to allow the individual to be identified. Examples include a person's name, address, social security number or e-mail address. Refer to Cal. Civ. Code § 56 *et seq.*

Contract Research Organization (CRO): an entity that assumes, as an independent contractor of the *sponsor*, one or more of the obligations of a sponsor, e.g., negotiation of contracts, design of a *protocol*, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the *FDA*.

Copyright: an exclusive right under federal law to copy, modify, distribute, perform and display a work of authorship, such as a book.

Covered entity: a health plan, health care clearinghouse, or health provider that transmits health information in electronic form. **HIPAA** protects the disclosure of **protected health information (PHI)** by covered entities without a person's consent. The University is a hybrid covered entity – as a health care provider, the University must comply with HIPAA's requirements regarding the disclosure of PHI to third parties. But, where the University uses PHI for internal research purposes, it need not comply with HIPAA. **Sponsors** are generally not covered entities.

Debarment: an action on entities and individuals, taken by the Secretary of Health and Human Services, which prevents such entities or individuals from assisting in the development of drug and device approval applications. A debarment can be based upon events such as a felony or misdemeanor that relates to the development or approval of drug applications, or a felony conviction that involves bribery, fraud, extortion or falsification of records.

Device: an instrument, apparatus, implement, machine, or diagnostic kit, which is intended for use in diagnosis, cure, mitigation, treatment or prevention of a disease or condition in man or animals. Devices do not achieve their primary purpose through chemical action within or on the body, nor are they dependent upon being metabolized for achievement of their purpose.

Drug: an article or compound (other than food) intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or animals.

Emergency use: Use of an **investigational drug, device or biological** on a **subject** with a life-threatening situation where standard treatment is not available and there is insufficient time to obtain full **IRB** approval.

Exclusion: an action on entities and individual health care providers, taken by the Secretary of Health and Human Services, which excludes such entities and individual health care providers from participating in federal health programs, such as Medicare or Medicaid. Exclusion can be based upon conduct such as Medicare or Medicaid fraud, patient abuse or neglect, felony convictions for other health care-related fraud, theft, financial misconduct, misdemeanor convictions relating to unlawful dispensing of controlled substances, submitting false claims to a federal health care program, or engaging in unlawful anti-kickback arrangements. If an entity or individual is excluded from Medicare or Medicaid, these programs may not cover costs that may traditionally be paid to entities or individuals for Medicare or Medicaid recipients participating in **clinical trials**.

Exclusive license: a legally enforceable promise wherein the owner of an **intellectual property** (e.g., a **patent**), authorizes, for a certain period of time, a person or entity to exclusively exercise one or more rights to that intellectual property. For example, the owner of a patent may exclusively license the right to manufacture a **patentable** invention. For the duration of the exclusive license, no one else may manufacture the patentable invention. However, the owner may grant an exclusive license to another entity to distribute or sell the intellectual property.

Food and Drug Administration: an agency of the U.S. Department of Health and Human Services. Its duties include approving **drugs** and **devices** to be used in **clinical trials** (through an **IND** or **IDE**) and approving the market sale and use of drugs and devices for an intended use following a **clinical trial**.

Health Insurance Portability and Accountability Act (HIPAA): a federal law, which, among other things, protects the disclosure of **protected health information** by **covered entities** without the patient's consent. Refer to Pub. L. 104-191.

HIPAA Authorization: document signed by a **subject** in a **clinical trial**, which authorizes the University (as a **covered entity**) to use and disclose their **protected health information** to third parties, such as the **sponsor** of the clinical trial. The University uses a standard form for all clinical trials conducted at the University.

Human subject: An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient (FDA Regulations 56.102 and 50.3 Definitions).

Indemnification: one party assumes financial responsibility in the event of a specified loss by another party; an indemnification clause transfers the risk of damages or loss from one party to the other party.

Indirect costs: the costs that cover facilities and administration. Facilities costs include the depreciation and use of buildings, capital improvements and equipment; interest on debt; and operation and management expenses. Administrative costs include departmental administration expenses that benefit common or joint departmental activities, general administrative expenses that do not solely relate to a major function of the University, sponsored projects administration and student administration and services.

Informed consent form: a form that must be signed by any participant in a **clinical trial**. The informed consent describes the purpose of the study, duration of the study, required procedures, risks, potential benefits, key contacts, and costs to **subject**, if any. The informed consent form must be reviewed by the

Institutional Review Board (IRB): Committee of academic institutions and medical facilities, which monitors human research studies. IRBs review, and approve of, research studies involving human **subjects** to assure the protection of rights and welfare of human subjects. IRBs are empowered by **FDA** regulations to approve and modify planned research studies, and therefore, review research studies before they begin and periodically during the research, to ensure that human subjects are protected. Specifically, IRBs review **protocols** and **informed consent** documents.

Intellectual property: refers to several types of creations of the mind for which a set of exclusive rights are recognized under the law. Under intellectual property law, owners are granted certain exclusive rights to a variety of intangible assets, such as musical, literary, and artistic works; discoveries and inventions; and words, phrases, symbols, and designs. Common types of intellectual property include **patents**, **copyrights**, **trademarks**, and **trade secrets**.

International Committee of Medical Journal Editors (ICMJE): A committee comprised of medical journal editors, which created requirements that **clinical trials** must meet in order for results to be published in their journals. Member journals include the New England Journal of Medicine, the Journal of the American Medical Association, and hundreds of others.

Intervention: Physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment performed for research purposes (45 CFR 46.102)

Investigational device exemption (IDE): permission from the FDA required for an entity to conduct a study (a **clinical trial**) on a device that has not yet been approved for use by the FDA. An approved IDE means that the **IRB**, and **FDA** for **significant risk devices**, has approved the **sponsor's** study application and will allow the device to be tested in a clinical study (refer to 21 CFR Part 812).

Investigational new drug (IND): permission from the FDA to conduct a study (*clinical trial*) on a *drug* that has not been approved for general use by the *FDA*, but is under investigation regarding its safety and efficacy, first by clinical investigators and then by practicing physicians using *subjects* who have given *informed consent* to participate. Sponsors seeking to use an IND must file an investigational new drug application with the FDA before it may be used in an investigation Refer to 21 CFR Part 312.

Investigator: an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the *drug* or *device* is administered or dispensed to a *subject*). In the event an investigation is conducted by a team of individuals, the investigator, or Principal Investigator, is the responsible leader of the team. “Subinvestigator” includes any other individual member of that team. **At USC**, all tenured, tenure track, and non-tenure track faculty, and research scientists (with the exception of lecturers, adjunct, and part-time clinical faculty) may act as Principal Investigators. Postdoctoral Research Associates and Postdoctoral Teaching Associates, as defined by USC’s Postdoctoral Scholars Policy, may act as co-principal investigators on sponsored projects, but may not be principal investigators unless a specific waiver and approval is granted upon recommendation by the Department and approval of the appropriate Dean.

Investigator-initiated: a study in which the Principal Investigator develops and conducts the *protocol*, and obtains an *IND* or *IDE*, if necessary. The *sponsor* provides funding and/or the *drug* or *device* to be studied in the *clinical trial*.

Investigator’s Brochure: a collection of data consisting of all the relevant information known prior to the onset of a *clinical trial* including: chemical and pharmaceutical data, toxicological, pharmacokinetic and pharmacodynamics data in animals, and the results of earlier clinical trials. There should be adequate data to justify the nature, scale and duration of the proposed trial. The information must be updated during the course of the trial, if new data arise.

Know how: knowledge developed with experience; not protected under federal or state law.

Medicare Coverage Analysis: A determination of the eligibility of a clinical study’s related tests, procedures, or interventions. The analysis requires a detailed review of the clinical events specified in the protocol to determine which can be reimbursed by Medicare in order to avoid improper billing and double-billing which can result in serious penalties. A Medicare Coverage Analysis review is necessary as part of the Research Billing Compliance process.

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(56 *CRF* 56.102).

Multi-center trial: a *clinical trial* conducted according to one single *protocol* in which the trial is takes place at different investigational sites, and is therefore carried out by more than one *investigator*, but following the same practical details.

Non-exclusive license: a legally enforceable promise wherein the owner of an *intellectual property* (e.g., a *patent*), authorizes, for a certain period of time, a person or entity the right to use intellectual property on a non-exclusive basis. For example, the owner of a patent may grant a sponsor the right to use a patent, but the owner may also grant others the right to use the same patent.

Partially completed subject: a *subject* that fails to complete all visits or procedures required pursuant to a *protocol*.

Patent: an exclusive right under federal law to prevent others from making, using, selling, offering for sale, or importing any product or service that incorporates the claimed invention. Patents are considered to be the most powerful form of *intellectual property* protection, enabling *sponsors* to prevent competitors from using their *drug* or *device* or similar drugs and devices that infringe the patent for the patient's lifetime.

Patentability (for a U.S. patent): an invention that meets the following criteria: (1) is of a kind of subject matter eligible for patent protection under federal law (i.e., a process, manufacture, or composition of matter or machine); (2) is novel; (3) is non-obvious; and (4) is useful. Refer to 35 U.S.C. § 101.

Payment Schedule: document specifying the *sponsor's* payments to the University based upon each procedure or visit completed on an individual study *subject*.

Phase I: the initial introduction of an *investigational new drug* into humans. They are typically closely monitored and may be conducted in patients or normal volunteer *subjects*. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, and the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase I, sufficient information about the drug's pharmacokinetic and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, *Phase II* studies. The total number of subjects and patients included in Phase I studies varies with the drug, but is generally in the range of 20 to 80. Phase I studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.

Phase II: controlled clinical studies conducted to evaluate the effectiveness of the *drug* for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase II studies are typically well-controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects.

Phase III: expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the *drug* has been obtained, and are intended to gather the additional information about effectiveness and safety needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase III studies usually include from several hundred to several thousand subjects.

Phase IV: conducted following a *drug's* approval from the *FDA* for a particular use and explore unapproved uses, dosages and indications of the drug.

Private information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject may readily be ascertained by the investigator or associated with the

information) in order for obtaining the information to constitute research involving human subjects (45 CFR 46.102).

Protected Health Information (PHI): individually identifiable health information of a person, that: (i) relates to the person's past, present or future physical or mental health condition, or the provision of health care to the individual; and (ii) identifies the individual or can be used to identify the individual's information. Examples include a person's name, address, birthdate and social security number. **HIPAA** protects the disclosure of PHI by **covered entities** without a person's consent.

Protocol: a document which states the rationale, objectives and statistical design and methodology of the **clinical trial**, with the conditions under which it is to be performed and managed. The following items are typically included in the protocol: statement of objectives and purpose; list of **investigators**, their qualifications, and each **IRB** that has approved the project; criteria for patient selection and exclusion and estimate of the number to be studied; description of the design of the study, control group to be used, if any, and the methods to be used to minimize bias on the part of **subjects**, investigators, and analysts; the method for determining the dose(s) to be administered, planned maximum dosage, and duration of patient exposure; observations and measurements to be made; and clinical procedures, laboratory tests or other measures to be taken to monitor the effects and minimize risk.

Raw data: **subject** data and results, which includes medical records of subjects, laboratory notes and other information collected by the University. The University may provide a compilation of raw data that is de-identified to **sponsors** and give sponsors ownership of the data as compiled to the sponsor. However, the University must own the raw data and be freely able to use the raw data it collects.

Reduction to practice: the filing of a **patent** application, or an invention that is sufficiently tested to demonstrate it will work for its intended purpose. In order to be **patentable**, an invention must be **conceived** and reduced to practice.

Registry agreement: an agreement for the purposes of enabling a pharmaceutical or device company to observe a health care provider's treatment of a patient using that company's drug or device. It enables the company to assess the **drug** or **device's** ability to achieve its intended use in the real world rather than pursuant to a **protocol**.

Research :A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities (45 CFR 46.102 – Protection of Human Subjects).

Research Order Form: A form used by the research staff to identify all services provided to subjects during a study and includes all clinical services identified by the protocol. The form functions as a physician order form requiring a physician signature, date and time.

Royalty: payment to the owner, usually based on a portion of sales, for the right to use **intellectual property** that is owned by another.

Screen failure: a **subject** evaluated for participation in a study who fail to meet the study's eligibility criteria.

Significant risk device: an investigational **device** that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a **subject**; (2) is for use in supporting or sustaining human life and represents a potential for serious risk to the health, safety, or welfare of a subject; (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (4) otherwise presents a potential for serious risk to a subject.

Sponsor: a person or entity taking responsibility for and initiating research or a clinical study. Sponsors fund the study and/or provide study materials. A sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private institution, or other organization. In **sponsor-initiated** trials at USC, the sponsor pharmaceutical or device company conceives of the design of the study. According to the FDA, the sponsor is also the holder of the IND – Investigational New Drug.

Sponsor-initiated: Sponsor creates the protocol, provides the drug or device, pays all costs of the trial and obtains **investigational new drug (IND) or investigational device exemption (IDE)** approval from the **FDA** to conduct the study. The Principal Investigator tests the drug or device pursuant to the sponsor's **protocol**.

Subject: a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or who participates as a control. A subject may be in normal health or may have a medical condition or disease.

Sub license: a license giving rights of production or marketing of products or services to a person or entity that is not the primary holder of such rights. For example, the University may provide a **sponsor** with a **non-exclusive license**, with the right to sublicense the invention to a business partner for the purposes of bringing the invention to market.

Total Direct Cost: indirect cost rate used for industry sponsored **clinical trials**. TDC rate includes equipment and other capital expenditures, charges for patient care and tuition remission, rental costs of space, scholarships and fellowships, and portions of subgrants and subcontracts in excess of \$25,000.

Trademark: a distinctive name, motto, symbol, or design that legally identifies a company or its products and services. A trademark protects others from using identical or similar marks and is protected by federal law.

Trade secret: intellectual property that the owner takes reasonable efforts to keep confidential, such as a customer list or business plan. Trade secrets are not generally known and give the owner a competitive advantage. Trade secrets are protected by state law; but, if the owner fails to take reasonable step to keep the information confidential, it is not subject to intellectual property protection. The University will not keep trade secrets confidential.

APPENDIX 7 - ACRONYMS

AAFRPP: Association for the Accreditation of Human Research Protection Programs

ACOSOG: American College of Surgeons Oncology Group

CDA: Confidential Disclosure Agreement

CFR: Code for Federal Regulations

CIC: Clinical Investigations Committee

CIRB: Central Institutional Review Board

CIRC: Conflict of Interest Review Committee

CISO: Clinical Investigations Support Office

CMS: Center for Medicare & Medicaid Services

CORES: Core Ordering and Reporting Enterprise System

CRF: Case Report Form

CRO: Contract Research Organization

CSA: Clinical Study Agreement

CTA: Clinical Trial Agreement

CTO: Clinical Trials Office

CTSU: Clinical Trial Support Unit

DLT: Dose Limiting Toxicity

DSCPRF: Disease Specific Clinical Program Review Form

DSMB: Data and Safety Monitoring Board

DSMC: Data and Safety Monitoring Committee

DSTL: Disease Specific Trial List

eCRF: Electronic Case Report Forms

FDA: Food and Drug Administration

FWA: Federalwide Assurance

GCP: Good Clinical Practice

GOG: Gynecologic Oncology Group

HHS: Department of Health and Human Services

HIPAA: Health Insurance Portability and Accountability Act

HRA: Health Research Association

HS: Human Subject

HSR: Human Subject Research

IB: Investigator's Brochure

ICF: Informed Consent Form

ICMJE: International Committee of Medical Journal Editors

ICOI: Institutional Conflict of Interest

IDE: Investigational Device Exemption

IIT: Investigator Initiated Trial

IND: Investigational New Drug

IP: Intellectual Property

IRB: Institutional Review Board

KC: Kuali Coeus

KFS: Kuali Financial System

LCD: Local Coverage Determination

MCA: Medicare Coverage Analysis

MCD: Medicare Coverage Database

MTD: Maximum Tolerated Dose

NCCC: Norris Comprehensive Cancer Center

NCD: National Coverage Determination

NCI: National Cancer Institute

NDA: Non-Disclosure Agreement

NSABP: National Surgical Adjuvant Breast and Bowel Project

OHPR: Office for Human Research Protections

OPRS: Office for the Protection of Human Subjects

PHI: Protected Health Information

PI: Principal Investigator

POC: Phase One Committee

PSC: Protocol Submission Checklist

QA: Quality Assurance

QAMC: Quality Assurance Monitoring Committee

RC: Research Coordinator

RIHSC: Research Involving Human Subject Committee of the Food and Drug Administration (FDA)

ROF: Research Order Form

RTOG: Radiation Therapy Oncology Group

SAE: Serious Adverse Event

SC CTSI: Southern California Clinical and Translational Science Institute

SIV: Site Initiation Visit

SNIF: Significant New Information Finding

SWOG: Southwest Oncology Group

TARA: Total Access for Research Administration