UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
AUDIT AND ADVISORY SERVICES

Clinical Trial Set-Up
Project #15-031

July 2015

University of California
San Francisco

UCSF

Audit and Advisory Services

July 16, 2015

Jennifer Grandis
Associate Vice Chancellor
Clinical and Translational Research

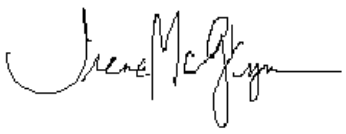
SUBJECT: Clinical Trial Set-Up

As a planned internal audit for Fiscal year 2015, Audit and Advisory Services (AAS) conducted a review of the clinical trial set-up process. Our services were performed in accordance with the applicable International Standards for the Professional Practice of Internal Auditing as prescribed by the Institute of Internal Auditors (the IIA Standards).

Our preliminary draft report was provided to department management in June 2015. Management provided us with their final comments and responses to our observations in July 2015. The observations and corrective actions have been discussed and agreed upon with department management and it is management's responsibility to implement the corrective actions stated in the report. In accordance with the University of California audit policy, AAS will periodically follow up to confirm that the agreed upon management corrective actions are completed within the dates specified in the final report.

This report is intended solely for the information and internal use of UCSF management and the Ethics, Compliance and Audit Board, and is not intended to be and should not be used by any other person or entity.

Sincerely,



Irene McGlynn
Director
UCSF Audit and Advisory Services

EXECUTIVE SUMMARY

I. BACKGROUND

As a planned audit for Fiscal Year 2015, Audit and Advisory Services (AAS) conducted a review to assess the adequacy of procedures and controls surrounding the clinical trials set-up process.

Effective June 2013, the University requires a formal coverage analysis to be completed for all UCSF's clinical trial studies. A formal coverage analysis is a systematic review of all clinical research items, services and procedures. It documents the appropriate funding source for each item or service, in accordance with relevant Federal and State medical billing regulations and policies. A coverage analysis must be completed prior to developing the study budget and enrolling study subjects. Effective July 1, 2014, University policy requires these coverage analyses to be completed in OnCore by one of the three approved coverage analysis offices. Units authorized to perform a formal coverage analysis are: the Clinical Trials Business Support Center (CTBSC), Investigational Trial Resource (ITR) and the Division of Cardiology. Between January 1, 2014 and January 31, 2015, the Committee on Human Research approved 177 clinical trials.

All expenses related to the conception, execution, and close-out of a clinical trial need to be captured and accounted for in the budget and billing processes. The signed Clinical Trial Agreement (CTA) dictates when and how UCSF may bill a sponsor. It is the source documentation for billing and takes precedence over any other communication or record.

In order to bill any payer besides the sponsor for routine care costs of items and services, a clinical trial must meet certain criteria to qualify for reimbursement. UCSF applies the Medicare National Coverage Determination for Routine Costs in Clinical Trials (NCD 310.1) to make this determination. Since clinical research often takes place concurrently with routine care, it is important that the billing for research and routine clinical activities are handled in accordance with the CTA and applicable regulatory requirements. Additionally, complete and accurate budgets help ensure that all UCSF incurred costs are accurately allocated to the appropriate responsible party, reducing the likelihood of budget shortfalls.

II. AUDIT PURPOSE AND SCOPE

The objectives of our review were to:

- Determine that protocol-specific budgets are developed to identify and capture all costs for conducting the study;
- Determine that Medicare coverage analysis is performed;
- Assess the adequacy of controls for accurate set-up of the trial within the OnCore system and APeX clinical research billing module;
- Determine that there is an appropriate review of documentation and approvals of, clinical trial studies; and
- Determine that there are consistent standards and quality review processes in place among the three groups for the set-up of clinical trials.

The scope of our review focused on the set-up processes for clinical trials and excluded clinical research billing related processes. Our testing population included new studies effective July 1, 2014, with the CTBSC, ITR and the Division of Cardiology.

Procedures performed as part of the review included: review of relevant policies, interviews with personnel and review of clinical trial documentation and coverage analysis. For more detailed steps, please refer to Appendix A.

Work performed was limited to the specific activities and procedures described above. As such, this report is not intended to, nor can it be relied upon to provide an assessment of compliance beyond those areas specifically reviewed. Fieldwork was completed in May 2015.

III. SUMMARY

Based on work performed, the studies appear to be accurately set-up in OnCore and APeX and there is appropriate review of study documentation for regulatory requirements. Processes for the development of study budgets and coverage analysis are in place and operating effectively.

Opportunities for improvement exist in the areas of establishing criteria for waiving clinical trial fees, the process to determine the costs of certain clinical procedures and services, consistency of documents uploaded to OnCore, and procedures to input the ClinicalTrials.gov identifier into OnCore.

The specific observations from this review are listed below.

- There are no defined guidelines for waiving of certain expenses related to clinical trial charges.
- Coverage Analysts do not have the necessary resources and tools to effectively determine the cost for certain clinical procedures and services.
- Among the offices that prepare coverage analysis, there is inconsistency with the set of documents uploaded to OnCore.
- The ClinicalTrials.gov identifier (i.e. NCT Number) was not always recorded in OnCore.

Additionally, during the course of this review, a potential opportunity for improvement was noted for enhanced process efficiency. Principal Investigator approval of the coverage analysis could be more consistently documented in OnCore among the groups.

IV. OBSERVATIONS AND MANAGEMENT CORRECTIVE ACTIONS

No.	Observation	Risk/Effect	Recommendation	Management Corrective Action (MCA)
1	***There are no defined guidelines for waiving of certain expenses related to clinical trial charges.*** Review of 11 studies found: • Administrative Fees: For one protocol of an industry sponsored study (EXPANDTRIAL), some administrative fees were waived by the PI (i.e. Study Team Startup and Close-out fee, and CHR application preparation fee, typically between $3000 - $6000). • Document Storage Fees: The budgets for three protocols (EXPANDTRIAL, UF and 147517) did not include Document Storage Fees (typically between $1000 - $1800). Per UCSF Administrative Policy 400-10: "Academic, Legal and Financial Policies of Contracts and Grants," it is The Regents' policy that extramurally funded projects are conducted at no cost to the University. All direct and indirect costs for extramurally funded projects must be recovered from the sponsor(s).	If an expense is not included in the budget of the signed contract, then it may not be billed to the sponsor, resulting in the University being responsible for those costs. Additionally, if fees are waived for some industry sponsors for their clinical trials, those sponsors may be charged less than federally funded studies.	Due to the nature of certain clinical trials, the University may want to waive some fees in order to make UCSF a more attractive site for the sponsors. However, criteria should be defined establishing the authority to waive fees associated with clinical trials and to recoup these costs from other sources. Additionally, the process for authorizing fee waivers should be established, including the reasoning for waiving fees.	All units preparing coverage analyses (i.e. CTBSC, ITR and Division of Cardiology) will include in their study budgets sufficient information to document the reasons and the funds that will cover expense waivers. This process will be implemented by July 31, 2015. The coverage analysis units will provide to AAS copies of any budgets with such waivers by September 1, 2015, for validation.
2	***Coverage Analysts do not have the necessary resources and tools to effectively determine the cost for certain clinical procedures and services.*** Coverage Analysts cannot effectively utilize	Clinical trial budgets may not fully capture all the costs if sufficient information is not available to those providing procedure costs for the budget.	1. Training should be provided to coverage analysts to better understand the fee schedules.	a) A new resource within the Research Billing team will be created and established to assist the coverage analysis units with creating budgets for

No.	Observation	Risk/Effect	Recommendation	Management Corrective Action (MCA)
	the clinical services research fee schedules to determine the expenses for incorporation in the study budget, specifically for complex procedures where all the components of the procedures may not always be known (e.g. several drugs and supplies may be required for an infusion). Also, they do not have an easy way of obtaining information on the professional fees for services. Therefore, they often have to rely on personnel from the Medical Center's Reimbursement Services for assistance in the creation of clinical trial budgets. However, the Reimbursement Services personnel may not always have all the relevant information, such as the study protocol, to ensure that correct and complete information is provided.		2. Develop a process and resource for obtaining information for complex procedures and professional fees.	clinical procedures and professional fees. By mid-June 2015, the job will be posted. The resource is expected to be in place by December 31, 2015. b) By March 31, 2016, a workgroup consisting of coverage analysis units and Medical Center's Reimbursement Services will perform an assessment aimed at developing a more efficient and simplified process for obtaining procedure costs for developing clinical trial budgets.
3	***Among the offices that prepare coverage analysis, there is inconsistency with the set of documents uploaded to OnCore.*** Other than the clinical trial protocol, some units do not load one or more of the following documents into OnCore: Informed Consent Forms, Related Manuals and Clinical Trial Agreements. Of the four clinical trials reviewed for ITR, none of them had IRB-approved informed consent forms or clinical trial agreements uploaded into OnCore. Additionally, for the six clinical trials reviewed for CTBSC and	OnCore is the system of record for clinical trials at UCSF. Having all necessary documents in a central repository permits efficient sharing of protocol information between the Study Team and the Coverage Analyst. If all required coverage analysis documentation is not appropriately stored, it may not be efficiently accessible to all stakeholders. In turn, this may affect decisions or	Together with Clinical Compliance, the three Coverage Analysis groups (CTBSC, ITR and the Division of Cardiology) should develop a standardized process by defining which documents should be retained in OnCore and ensure that these are maintained.	By October 31, 2015, together with Clinical Compliance, the three Coverage Analysis groups (CTBSC, ITR and the Division of Cardiology) will develop a standardization for documents housed in OnCore.

No.	Observation	Risk/Effect	Recommendation	Management Corrective Action (MCA)
	the one reviewed for Cardiology, no related manuals (e.g. Investigator's Brochure) were loaded into OnCore. Per the Coverage Analysis Standard Operating Procedure (6/1/14): coverage analysis documentation is uploaded to OnCore and will include: the final protocol, IRB-approved informed consent(s), related manuals, clinical trial agreement and supporting justification for all billing determinations.	actions taken using incomplete or out of date information.		
4	***ClinicalTrials.gov identifier (i.e. NCT Number) was not always recorded into OnCore***. Of the 11 protocols reviewed, we noted that the NCT number for two (protocols IVIG-Registry and 142011) were not recorded in OnCore. The trials are registered on ClinicalTrials.gov; however, the NCT number for these trials are not noted in OnCore. Effective January 1, 2015, Center for Medicare and Medicaid Services (CMS) requires the study to be registered on ClincialTrials.gov and a NCT Number to be reported on all billing claims for items and services related to qualifying clinical trials.	In the future, it is projected that there will be an interface between OnCore and APeX for billing purposes. The lack of the NCT number in OnCore may create potential issues in identifying transactions as study charges for payment.	Generally, a clinical trial sponsor will register their study on the ClinicalTrials.gov website. Procedures should be developed and implemented to help ensure that the NCT Number is recorded in OnCore so that there is complete information for billing of research studies.	a) By August 31, 2015, the coverage analysis units will communicate the expectation that the NCT number is entered into OnCore to the relevant personnel via the CRC listserv. b) By September 30, 2015, the feasibility of creating a monitoring report of missing NCT Numbers from OnCore will be explored. If report can be produced, the missing NCT number report will be sent quarterly to relevant PIs to obtain the required data and enter it into OnCore.

V. OPPORTUNITY FOR IMPROVEMENT

No.	Observation	Risk/Effect	Recommendation
1	***The documentation of PI's approval of the final coverage analysis could be improved through implementing e-signature***. Principal Investigators are ultimately responsible for all aspects of conduct the research study, including financial aspects. Generally, the PI's approval of the coverage analysis is made via email and retained in the study files or in OnCore. An electronic signature application may be an efficient and effective solution to manage routing of the coverage analysis and document the approval by the PI's. (DocuSign is UCSF's e-signature solution)	As OnCore is the system of record for coverage analysis, it may be more appropriate and accessible to document the PI's approval of the final coverage analysis in OnCore, rather than having the email retained by the study team.	DocuSign is UCSF's e-signature solution and consideration should be given to utilizing this electronic signature application for effectively routing of the coverage analysis and documenting the approval by the PIs.

APPENDIX A – Procedure Steps

To conduct our review the following procedures were performed for the areas in scope:

- Reviewed relevant UCSF Administrative Policies, including: Policy 100-36: Clinical Trials Registration & Reporting and Policy 100-16: Research Involving Human Subjects;
- Interviewed key department personnel from CTBSC, ITR and the Division of Cardiology;
- Reviewed the budgets, Committee on Human Research (CHR) approvals, and CHR approved informed consent forms for a sample of 11 studies;
- Performed an analysis of data from OnCore to determine if any studies were initiated prior to CHR approval;
- Verified that budgets were complete and accurately captured costs for conducting the study;
- Reviewed the coverage analysis for a sample of studies (performed by Clinical Compliance);
- Validated that the sample of trials have been accurately set up in OnCore and APeX and were registered on the federal government website, ClinicalTrials.gov.