

Standard Operating Procedure (SOP)
Office of Research Services
Review of Budgets, Contracts and Consent Forms for Industry-Initiated, Industry-Sponsored Clinical Trials Research

Introduction

The institution encourages interactions and research with the private sector, and understands that such interactions are essential to achieving our mission and goals.

In general, sponsors of clinical trials are expected to pay all study-related expenses that are not covered by other third party insurers. Federal guidelines (summarized in Appendix A) clearly indicate that certain clinical services provided as part of an industry sponsored clinical trial may be billed to government payers. There are also guidelines clearly stating that certain services which are not standard of care and thus are not billable to third party insurers not be billed to study participants. In order to comply with these guidelines, investigators, coordinators and other individuals involved in health care operations processes must know:

- if a patient is participating in a study; and
- if the services they are providing are part of the study and/or standard of care.

In addition, there are certain start-up costs (IRB submission, budget preparation, and consent preparation fees) that must be included in all industry sponsored clinical trials research contracts and budgets.

As a result of these requirements, the following procedures must be followed for every proposal submitted for industry sponsored clinical trials research. These procedures do not replace or provide relief from processes required by the IRB, SSOM Grants Administration or LUMC Finance.

Proposal Submission Requirements

When working towards the initiation of an industry sponsored clinical trial, a copy of the proposal/protocol provided to the IRB must also be submitted to the Central Clinical Trials Office (CCTO) together with the following information:

- Study Routing Form
- Sponsor Contract
- Protocol
- Detailed budget based on costs for services provided (should be e-mailed to CTO@lumc.edu unless budgetary preparation is to be done by the CCTO)
- Letter accepting responsibility for SOC designation (see Appendix B)
- Detail of Standard of Care (SOC) indicated on the study budget (see Appendix C)

The CCTO will review the information and provide advice on modifications that may have to be made in the budget. The local standard of care indication is required for every clinical service provided. This is mandatory for billing and compliance with regulations (see Appendix A).

Budget Preparation and Negotiation

Approval of the budget by the CCTO is required prior to an investigator's negotiation of financial terms with an industry sponsor. A budget preparation fee of \$1,000 will be charged to all industry trials. The PI will retain this fee when the **detailed budget** is prepared by the PI (or his/her coordinator/business manager) and requires minimal review by the CCTO. If the PI requests the CCTO to prepare the budget, the fee will be retained by the CCTO, and the PI will be required to review and approve the budget as prepared. In addition, if the CCTO requires more than minimal time and effort (~ 1.5 hour) to review and correct a budget prepared by the PI's office, the CCTO will charge 50% of the budget preparation fee (\$500).

Fixed Costs:

There are fixed costs that are applicable to all industry sponsored clinical trials studies. These must be incorporated in the budget. They are:

Budget Preparation Fee*	\$1,000
Consent Preparation Fee* (if applicable)	\$1,000 (plus \$500 for each additional language)
Set-up Fee* (initiation, education and template design)	\$1,000
Advertisement Fee	as appropriate
Pharmacy Fee* (if applicable)	\$ 550
Pharmacy Annual Review* (if applicable)	\$ 160
IRB Fee	\$ 3,000
Indirect Cost % (on all costs except IRB Fee)	26%

*(subject to 26% overhead)

All industry-sponsored trials will be required to pay a one-time IRB fee of \$3,000, which covers annual reviews and amendments. This fee is assessed by the Office of Research Services (ORS) for the review of protocols submitted to the IRB. The IRB does not set the fee, nor does it have the authority to waive the fee. This fee is not transferred to the CCTO. If the trial work is performed by the CCTO, the CCTO will bill the sponsor for the IRB fee as well as all other expenses related to the trial. If the trial is managed by a department, it is the department's responsibility to bill the sponsor for the IRB fee as well as all other expenses related to the trial. The Office of Fiscal Affairs will insure that the IRB fee is transferred to the IRB account from the initial sponsor payment.

PI initiated clinical trials studies (phases 1–4) that are not funded during the IRB's initial review but receive subsequent industrial funding will also be required to pay the entire IRB fee (\$3,000) unless a lesser fee is approved by the Senior Associate Dean for Research.

Subject-Related Costs:

The following information is required for subject-related costs:

1. Each physician, hospital and pharmacy service provided with CPT codes when appropriate;
2. Frequency of the service;
3. Salary plus fringe benefits for staff working on the study; and
4. Indirect costs (IDC) calculated on all budget categories including patient care
 - a. Exclusion from IDC: IRB fee.

Appendix C provides a spreadsheet that may be useful for preparing detailed budget proposals for clinical trials research.

Budget proposals may be denied or refused by the CCTO and returned to the investigator if the data requested above are not provided.

A budget approved by CCTO is the baseline for negotiations. The PI or his/her agent may negotiate a higher budget with the sponsor, but may not accept a budget lower than that approved by the CCTO.

Payment Processing and Budget Management

To ensure that appropriate internal controls are in place, new award account setups and all payment activity for industry sponsored clinical trials will be centralized in the Fiscal Affairs Office regardless of whether the CCTO or Department manages the project.

1. All invoicing to the sponsor is the responsibility of the manager (e.g. coordinator or business manager) of the trial.
2. All payments (checks) are made payable to Loyola University Chicago (LUC) and forwarded to the Office of Fiscal Affairs (Building 120) with the required information identifying the study (proposal submission requirements). (LUC Tax ID – 361408475)
3. The trial manager or their designee will enter all payments and the appropriated budget into the Research Channel.
4. New award set up will require the following to be submitted to the CCTO:
 - a. Fully executed agreement (LUC and sponsor signatures) including all addendums, appendices and attachments describing the financial terms of the contracts;
 - b. CCTO approved budget;
 - c. Signed routing form; and
 - d. Check and LU# reference.

5. The Fiscal Affairs Office will approve the appropriation distribution in the Research Channel, scan the check and supporting documents, and forward the data to SPA for processing.
 - a. SPA will receive a copy of the routing form, budget appropriation, fully executed agreement (for new awards) and other supporting documentation.
 - b. The scanned documents and date sent to SPA will be available for viewing in the Research Channel.
 - c. The Fiscal Affairs Office will verify that checks are deposited, funds are appropriated and related fees are paid.
 - d. SPA will not process new grant accounting unit (AU) requests from SSOM unless they are submitted by the Grants Administrator in Fiscal Affairs.

6. Subsequent payments require the following to be submitted to the Fiscal Affairs Office:
 - a. Supporting documentation (invoice, budget and sponsor correspondence if available); and
 - b. Check and LU# reference.

7. All requests for close outs of clinical trials should be submitted to the CCTO (see appendix D).

Consent Preparation

A Consent Preparation Fee is charged for all industry sponsored trials (see Appendix C). This fee can be retained by the PI if the consent is prepared by the PI (or his/her coordinator/business manager) and requires minimal review by IRB staff. If the IRB staff requires more than minimal time and effort to review the consent (~ 1 hour), the IRB Office will charge 50% of the Consent Preparation Fee (\$500). Alternatively, the PI may request that the consent be prepared by the IRB staff and pay the entire Consent Preparation Fee to the IRB Office. The Office of Fiscal Affairs will insure that appropriate payments are made to the IRB account.

Contract Review

All contracts for research must be approved by the Senior Associate Dean for Research after review by the ORS Staff Attorney. The proposed industry contract should be forwarded to the Staff Attorney (electronically with all necessary information as described on the Staff Attorney checklist) when the protocol is submitted to the IRB, thus allowing both reviews to occur simultaneously. The Staff Attorney will review the contract (excluding the budgetary component) and negotiate all terms with the industry sponsor. Once approved, the contract will be submitted to the Senior Associate Dean for Research, who will sign the contract after IRB approval and budgetary approval are documented.

APPENDIX A

Summary of Regulatory Guidance

(excerpts taken from National Coverage Decision on Clinical Trials, effective 09/19/2000 and National Coverage Decision on Investigational Devices, published 09/01/1996)

A National Coverage Decision was issued effective September 19, 2000 based upon the authority found in §1862(a)(1)(E) of the Social Security Act (Act). It is binding on all Medicare carriers, fiscal intermediaries, Peer Review Organizations, Health Maintenance Organizations, Competitive Medical Plans, Health Care Prepayment Plans, and Medicare+Choice organizations (§1852(a)(1)(A) of the Act). An administrative law judge may not disregard, set aside, or otherwise review a National Coverage Decision issued under §1862(a)(1) of the Act. 42 C.F.R. §405.860.

Under this decision, Medicare covers the routine costs of qualifying clinical trials, as well as reasonable and necessary items and services used to diagnose and treat complications arising from participation in all clinical trials. Routine costs of a clinical trial include all items and services that are otherwise generally available to Medicare beneficiaries that are provided in either the experimental or the control arms of a clinical trial except:

- The investigational item or service, itself;
- Items and services provided solely to satisfy data collection and analysis needs, and that are not used in the direct clinical management of the patient (e.g., monthly CT scans for a condition usually requiring only a single scan); and
- Items and services customarily provided by the research sponsors free of charge for any enrollee in the trial.

Routine costs in clinical trials include:

- Items or services that are typically provided in the absence of 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-covered chemotherapeutic agent), for clinically appropriate monitoring of the effects of the item or service, or for 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.

Requirements for Medicare Coverage of Routine Costs

Any clinical trial receiving Medicare coverage of routine costs must meet the following three requirements:

1. The subject or purpose of the trial must be the evaluation of an item or service that falls within a Medicare benefit category (e.g., physicians' service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids).

Appendix A (cont.)

2. The trial must not be designed exclusively to test toxicity or disease pathophysiology. It must have therapeutic intent.
3. Trials of therapeutic interventions must enroll patients with diagnosed disease rather than healthy volunteers. Trials of diagnostic interventions may enroll healthy patients in order to have a proper control group.

However, the three requirements above are insufficient by themselves to qualify a clinical trial for Medicare coverage of routine costs. Clinical trials should also have the following desirable characteristics:

1. The principal purpose of the trial is to test whether the intervention potentially improves the participants' health outcomes;
2. The trial is well-supported by available scientific and medical information, or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
3. The trial does not unjustifiably duplicate existing studies;
4. The trial design is appropriate to answer the research question being asked;
5. The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully;
6. The trial is in compliance with Federal regulations relating to the protection of human subjects; and
7. All aspects of the trial are conducted according to the appropriate standards of scientific integrity.

Some trials are presumed to meet the desirable characteristics and are automatically qualified to receive Medicare coverage. Effective September 19, 2000, clinical trials that are deemed to be automatically qualified are:

1. Trials funded by NIH, CDC, AHRQ, CMS, DOD, and VA;
2. Trials supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD and VA;
3. Trials conducted under an investigational new drug application (IND) reviewed by the FDA; and
4. Drug trials that are exempt from having an IND under 21 CFR 312.2(b)(1) will be deemed automatically qualified until the qualifying criteria are developed and the certification process is in place. At that time the principal investigators of these trials must certify that the trials meet the qualifying criteria in order to maintain Medicare coverage of routine costs. This certification process will only affect the future status of the trial and will not be used retroactively.

Medicare will cover the routine costs of qualifying trials that either have been deemed to be automatically qualified or have certified that they meet the qualifying criteria unless CMS's Chief Clinical Officer subsequently finds that a clinical trial does not meet the qualifying criteria or jeopardizes the safety or welfare of Medicare beneficiaries.

Appendix A (cont.)

For trials that do not have deemed approval status, the Agency for Healthcare Research and Quality (AHRQ) convened a multi-agency Federal group composed of representatives of the Department of Health and Human Services research agencies (National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), AHRQ, and the Office of Human Research Protection), and the research arms of the Department of Defense (DOD) and the Department of Veterans Affairs (VA). This multi-agency group will develop qualifying criteria that indicate a strong probability that a trial exhibits the desirable characteristics listed above. These criteria should be easily verifiable and where possible dichotomous. The multi-agency group will not approve trials. Trials that meet the qualifying criteria developed by the multi-agency group will receive Medicare coverage of their associated routine costs. The qualifying criteria will be developed under the authority found in §1142 of the Social Security Act (Act) (cross-referenced in §1862(a)(1)(E) of the Act).

For unqualified or non-certified trials, the trial's principal investigator must submit a certification form indicating which of the qualifying criteria the trial meets and a copy of the trial protocol to a Medicare clinical trials registry. If the completed certification form demonstrates that the trial meets the criteria, the registry assigns a trial identifier to it. This identifier would allow the routine costs of the trial to be billed to Medicare. The Medicare clinical trials registry is designed to protect patient confidentiality.

The regulations on investigational devices found in 42 C.F.R. §405.201-405.215 and §411.15 and §411.406 refer to two categories of devices being studied in clinical trials under Investigational Device Exemptions (IDE). The FDA will place all approved IDEs into one of these two categories:

Category A - Experimental/Innovative devices consist of:

1. Novel, first-of-a-kind technologies;
2. Innovative devices for which the absolute risk of the device type has not been established and initial questions of safety and effectiveness have not been resolved;
3. Devices believed to be in Class III; and
4. Devices for which the FDA can not insure safety and effectiveness.

These devices are not covered under Medicare. They do not satisfy the statutory requirement that Medicare pay for devices determined to be reasonable and necessary.

Category B- Non-experimental/Investigational devices consist of:

1. Devices that are newer generations of proven technologies;
2. Devices believed to be in Classes I or II;
3. Devices in class III, where the incremental risk is the primary risk in question (i.e., the underlying questions of safety and effectiveness of that device type have been resolved). It is known that the device type can be safe and effective because, for example, other manufacturers have obtained FDA approval for that device type;
4. Devices where initial questions of safety and effectiveness have been resolved; and
5. Devices considered to represent evolutionary changes in proven technologies

Appendix A (cont.)

These devices may be considered reasonable and necessary and, therefore, may be covered if all other applicable Medicare coverage requirements are met.

Billing Guidance for Devices

The FDA issues a special identifier number that corresponds to each device granted an Investigational Device Exemption (IDE). This number must be indicated on all claims. Detailed guidance was provided to providers and carriers on modifier usage, appropriate ICD-9 codes and billing instructions for the claim forms on a line-by-line basis. The guidance also indicated “the billing provider must include in the beneficiary's medical record the following information: trial name, sponsor, and sponsor-assigned protocol number. This information should not be submitted with the claim but must be provided if requested for medical review. A copy of the signed informed consent document must also be made readily available if requested for medical review”.

APPENDIX B

Date:

From: Dr. X (Principal Investigator); _____
Signature of PI

To: Central Clinical Trials Office (CCTO)

Re: Project title (LU#)

I have reviewed the proposed budget submitted for the above noted study. Items in the budget that are designated “Standard of Care” would be provided for all non-study patients presenting with the conditions/diseases of the subjects included in this study, and thus should be reimbursable by third party payers. I understand that items listed as “Standard of Care” that are not reimbursable by a third party will be billed to the study budget or other institutional sources.

APPENDIX C

LU#							
Sponsor:							
Title:							
PI:							
					Indirects 26%		
FIXED FEES - INITIAL							
Consent Preparation Fee	\$1,000.00	+ \$500 per	additional	language		+	
Budget Preparation Fee	\$1,000.00					+	
Set-up Fee (initiation and template)	\$1,000.00					+	
Pharmacy Review	\$ 550.00					+	
IRB Fee	\$3,000.00						
Advertisement costs (as appropriate)							
FIXED FEES - ANNUAL							
Pharmacy Annual Review	\$ 160.00	annually				+	
STUDY COSTS PER PATIENT/SUBJECT							
For each study visit list procedures and tests together with CPT codes, costs, number of events and whether it is standard of care include 26% IDC on all subject/study costs							
	CPT code	Cost	# Events	SOC	Indirects 26%	Total	
Visit - name (e.g. screening)							
Procedure/tests - listed individually							
Subtotal Study Costs Per Patient Costs							
PERSONNEL COSTS PER PATIENT/SUBJECT (including data handling)							
For each nurse/coordinator involved in the study, list hourly rate and hours required; include both salary and fringe benefits include 26% IDC on salary and fringe benefits							
	Hourly	Hours	Subtotal		Indirects 26%	Total	
Two rows (one salary and one fringe benefits) for each individual							
Subtotal Salary, Benefits, Indirect Costs							
Total Per Patient Study Costs							

OFFICE OF RESEARCH SERVICES
CLINICAL TRIAL PROJECT CLOSEOUT FORM

Accounting Unit _____ LU _____

PI Name _____ Department _____

Funding Source _____

Title: _____

Signature Approvals

PI _____ Date _____

The PI's signature indicates that the study is terminated and all study-related bills have been paid.

Final Notifications

Signature and date

Department
Administrator _____

Central Clinical Trials
Office _____

Disposition of Remaining Funds

Send completed form to Central Clinical Trials Office, Bldg. 54, Room 067