

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT HOUSTON
Office of Sponsored Projects
Standard Operating Procedures

Category: Contracting	
Title: Clinical Trial Contracting Guidelines	
Date First Effective: 8/22/06	Revision Date: 11/07/07

POLICY

The University of Texas Health Science Center at Houston (UTHSC-H) complies with federal, state and local law and conforms its processes to the contracting requirements of The University of Texas System, **Office of General Counsel**. In addition, UTHSC-H strives to be in accordance with Association of American Medical Colleges (AAMC) guidelines in clinical research contracting.

OBJECTIVE

This Standard Operating Procedure (SOP) describes the Office of Sponsored Projects (OSP) guidelines for clinical trial contracting. *This guide is not meant to be a comprehensive tutorial on contract review or contract administration; but rather, its focus is a quick review of the most frequent points of concern and confusion to principal investigators (PI) and their administrators regarding contract administration in sponsored projects.*

APPLICABLE REGULATIONS AND GUIDELINES

The University of Texas System, Office of General Counsel
CPHS Guidelines, Research Related Injuries
UTHSC-H Clinical Research Budgeting and Billing Program Business Process
HOOP 11.07
IRB Fees
The University of Texas System, Office of General Counsel, Master Agreements

ATTACHMENTS

N/A

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Clinical Trial Contracting Guidelines

Execution of Clinical Trial Agreements (CTA)

UTHSC-H faculty and staff participate in numerous clinical trial projects to answer specific questions about new medical treatments (medicine/drug, medical device, new therapies, vaccines), or new ways of using known treatments. Clinical trials (also called medical research and research studies) are conducted under highly-controlled conditions and used to determine whether such new treatments are both safe and effective. These studies are usually funded by pharmaceutical companies and are an important part of the process to ensure the safety and efficacy of the drug or device, obtaining Food and Drug Administration (FDA) approval and bringing a product to market.

OSP is responsible for reviewing, negotiating and legally executing CTAs from external funding sources. The resolution of many contractual issues requires coordination between the external funding source, PI and OSP; the involvement of each party is essential to a successful CTA with mutually acceptable terms. PIs should provide OSP with a copy of the proposed CTA, **Review and Approval Form** (R&A Form), copy of the protocol, and a company contact person as early in the process as possible. Committee for the Protection of Human Subjects (CPHS) (Institutional Review Board IRB) approval is not required in order for OSP to execute a CTA. To expedite the process even before submitting an **R&A Form**, the company contact may send the CTA electronically to the Contracts Sections of OSP.

Although each CTA is reviewed on a case-by-case basis, there are a number of key issues that are common to most CTAs. The following items will be negotiated by the OSP with the Sponsor:

Parties to the CTA

All CTAs will be between The University of Texas Health Science Center at Houston and the Sponsor. The PI is an employee of the UTHSC-H and cannot contractually bind the UTHSC-H.

Indemnification

The sponsoring company, and the actual owner of the study drug or device if an intermediary (Contract Research Organization) is involved, must agree to indemnify and hold harmless the UTHSC-H, The University of Texas System, its Board of Regents, PI, officers, agents and employees from any and all liabilities, claims, actions or suits for personal injury or death arising from the administration of the study drug, including but not limited to the use of the study results by Sponsor. To the extent authorized by the Constitution and laws of the State of Texas, the UTHSC-H will indemnify the Sponsor for negligent activities.

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Subject Injury, CPHS Guidelines:

<http://www.uth.tmc.edu/orsc/irb/guidelines/index.html>

OSP defers to CPHS for all subject injury related matters. The costs for care of a research-related injury when a subject is enrolled in a study sponsored by a commercial company (pharmaceutical company, device company, etc.) MUST be covered by the company. OSP will not approve language in the CTA, nor will CPHS approve wording in a consent form that indicates that the sponsor will pay for research-related injury only if the subject's insurance denies payment. The UTHSC-H does not bill the subject's insurance for research related costs.

Data Safety and Monitoring Boards (DSMB)

UTHSC-H and Sponsor shall promptly notify each other upon identifying any aspect of the study protocol, including information discovered during site monitoring visits or the study results, that may adversely affect the safety, well-being, or medical care of subjects, or that may affect the willingness of subjects to continue participation in the study, influence the conduct of the study, or that may alter CHPHS approval. When possible, the Sponsor shall submit such findings UTHSC-H electronically. UTHSC-H or the PI will promptly notify CPHS of any such events. When participant safety or medical care could be directly affected by study results, UTHSC-H will send participants a written communication about the results.

Sponsors are required to provide CPHS copies of any data and safety monitoring reports related to the study, including any reports of any independent data and safety monitoring committees.

Confidentiality

It is often necessary for the sponsor to provide information of a proprietary nature (the protocol) to the PI or his/her staff and it is important to the company's business interests that the confidentiality of this information be protected. Written confidential information should be stamped as such and oral communication should be reduced to writing and stamped "confidential" within thirty (30) business days of disclosure. Access to confidential information (including the protocol) must be strictly controlled and each PI should have a plan for ensuring confidentiality. All CTAs must have a time limit for information to be kept confidential by UTHSC-H. Our standard language is to allow information received from the Sponsor to be kept confidential for a period of three (3) years after the termination of the CTA. The following exceptions to the confidentiality section are included in the CTA: 1) is not disclosed in writing or reduced to writing and so marked with an appropriate confidentiality legend within thirty (30) days of disclosure; 2) is already in the recipient party's possession at the time of disclosure thereof; 3) is or later becomes part of the public domain through no fault of the recipient party; 4) is received from a third party having no obligations of confidentiality to the disclosing party; 5) is independently developed by the recipient party; 6) is disclosed for the safety and well-being of the subject or 7) is required by law or regulation to be disclosed.

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Publication

The CTAs must allow the PI the freedom to publish results of the study. However, the sponsor may have the right of prior review (without reference to “approval” or “consent”) to identify proprietary or confidential information.

Intellectual Property

The drug or device being tested in a clinical trial is typically owned by the sponsoring company and already covered by patent protection. Although each situation must be reviewed on its own merit, the **Board of Regents Rules** provide that title to inventions arising from projects conducted by faculty, staff or students will be owned by the Board of Regent’s. CTAs usually afford the sponsor the right of first refusal to obtain an exclusive, worldwide, royalty-bearing license to inventions arising from the conduct of the study.

Insurance

To support its indemnification obligations under the CTA, the sponsor must maintain a sufficient level of insurance. Each component of The University of Texas System is self-insured pursuant to The University of Texas System Medical Liability Benefit Plan (Plan), a self-insured plan under the authority of Section 59.01 of the Texas Education Code. The Plan covers the clinical faculty at the Medical School and Dental Branch, as well as the students and residents of the Medical School and Dental Branch.

Governing Law

CTAs must either be governed by the laws of the State of Texas or the governing law provision must be absent from the CTA.

Generic Drug Enforcement Act

Many CTAs include a clause which requires a certification that the PI and others participating in the study are not debarred, and have never been debarred, under the Generic Drug Enforcement Act of 1992. The UTHSC-H must notify the company of any debarment or threat of debarment occurring during the term of the study and usually one year afterwards. PIs and other staff members in the study may be required to sign such a certification.

Clinical Trial Master Agreements

Master Agreements are agreements that embody agreed-upon terms and conditions of a basic relationship between The University of Texas System institutions and a sponsor. Once a **Master Agreement** is in place, an "addendum" or "study letter" is generated for each new study to be conducted under this **Master Agreement**. The Addendum sets forth the items particular to a certain study such as the protocol name, the PI and the payment terms/amounts. The Addenda are "attached" to the **Master Agreement**. This alleviates the need to "reinvent the wheel" for each agreement; as the major terms are agreed upon and only the particulars need to be negotiated. We currently have many Master Agreements

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in place and The University of Texas System, Office of General Counsel is currently working on several more.

Budgets and Funding

PIs are responsible for following the **UTHSC-H Clinical Research Budgeting and Billing Program Business Process** when developing the study budget. The negotiated budget should be in the best interest of the UTHSC-H. All costs necessary to conduct the study, including salaries, supplies and indirect costs, should be considered when determining the fixed per-patient amount. Sponsors usually use one of two options when presenting a budget. They may offer a certain amount per patient and ask that you work within that amount or they may ask you to formulate a budget for them. Regardless, it is the PIs responsibility to ensure that the amount agreed upon will adequately cover all costs associated with conducting a clinical trial. OSP will not review budgets when negotiating the agreement with the sponsor. OSP will evaluate your budget for compliance with indirect cost policies to ensure that your budget falls within institutional guidelines.

Indirect Costs

HOOP 11.07, Indirect Costs

Indirect costs for human clinical studies are assessed at the flat rate of 30% of total direct costs (including IRB fees and startup costs). To estimate indirect costs when the direct costs are known, add 30% of the direct costs. The sum of these two figures is the per-patient amount. Example: If \$1,000 is needed to cover direct costs, 30% or \$300 should be added for indirect, bringing the total to \$1,300 per patient.

Basic Indirect Cost Recovery Example:

\$1,000 check received from sponsor for a clinical trial.

Calculation: $\$1,000/1.30 = \769.23 Direct Cost

IRB Fees

IRB fees are required for the review of new protocols and annual continuing review applications for clinical studies of drugs and devices sponsored by pharmaceutical companies and other for-profit entities. Fees will not be charged for Federal, non-profit foundations, or investigator-funded studies.

On contracts greater than \$50,000 = \$1,500

On contracts less than \$50,000 = \$1,000

On continuing contracts = \$300

On contracts less than \$5,000 = phone CPHS office to determine if a waiver is possible.

NOTE: Indirect Costs (30%) will be charged on all **IRB fees**.

IRB fees will be invoiced to the PI at the time protocols are set for review on the agenda of the review committee. **IRB fees**, along with the associated indirect costs, should be included as a line item in the budget as an upfront, non-refundable item. All fees are the responsibility of the PI.

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Payment Schedules for Clinical Trials

Sponsors will usually specify certain milestones that must be achieved before payment is made. Pay close attention to the timing and requirements of the milestones. Payment schedules may be appended to the contract as a table or may be written as a paragraph within the contract. Sponsors will oftentimes want to pay us at the end of the project versus the beginning of the project. The majority of the work will occur at the beginning of the trial and UTHSC-H should be paid accordingly.

A preferred payment schedule would be:

Payment No.	Milestone	Payment Amount
1	Initial Payment and/or non-refundable start-up fees + IRB fee upon contract execution	\$5000
2	After 3 subjects randomized	\$7500
3	After 2 subjects completed	\$5000
4	After 2 subjects completed	\$5000
5	Final payment after all Case Report Forms are completed, queries are resolved and close out visit is complete	\$2500

The Research Coordinator should ask for a reasonable initial payment that will cover the startup costs, preferably non-refundable. This amount should be adequate to cover all direct and indirect costs incurred with initiating a trial including the **IRB fee** in the event that the trial never begins.

Review the milestone payments. Will the UTHSC-H be paid on completion of Case Report Forms (CRF)? That may mean waiting until the monitor has reviewed the CRF's and sent them into data management. Will UTHSC-H be paid on completion of a subject's participation in the trial? This may delay payments. An ideal schedule will reimburse after a reasonable amount of subjects have been randomized or after a certain number of visits are completed so that your study account does not run in a deficit.

Sponsors may also choose to hold back a significant portion of payment until all study activities are complete. Ensure that this is not an excessive amount. No more than 10% of the total budget is ideal. Final payment may or may not depend upon waiting until ALL sites are closed or until the database has been closed. Pay close attention to this because it could delay receipt of final payment for an unreasonable amount of time.

An ideal payment schedule would include the following:

- Non-refundable initial payment that includes IRB fee and startup costs

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- Regular payments with realistic milestones
- Final payment made upon closure at your site
- Invoicing permitted for other costs (i.e. equipment, advertising)
- Screen failures and early termination
- Not every subject enrolled in a trial will complete the trial. Ensure that the budget and payment schedule provide for these circumstances adequately.

W-9, IRS Identification, and Payment Information

Tax ID# 74-1761309

OSP prepares all W-9 forms requested by sponsors as the form requires institutional signature. The member institutions of the University of Texas System are not tax exempt under the provisions of Internal Revenue Code (IRC) Section 501 (c)(3). However, the UTHSC-H is exempt as part of the State of Texas under Section 115 of the Internal Revenue Code.

Checks from the sponsoring company should be made payable to The University of Texas Health Science Center at Houston and mailed to The University of Texas Health Science Center at Houston, P.O. Box 203382, Houston, TX 77216-3382, Attn: FAST Team.

Clinical Trial Project Number (FMS Account Number) Establishment

To obtain a UTHSC-H project number (FMS account number) for a clinical study the following documentation is required: a completed and signed **R&A Form**, study budget, a fully executed agreement between the sponsoring company/agency and the UTHSC-H, CPHS approval. Funds are added to the project account as received.

Clinical Trial Project Close-Out

At the conclusion of any clinical trial study there may be a cash balance remaining. If expenditures incurred to conduct the study are reasonable in relation to the projected cost and when all costs (direct and indirect) have been properly charged and documented, the cash balance will be made available to the PI or his/her Department.

Clinical Trial Amendments

An amendment changes the terms of a previously executed agreement. If the amendment increases the dollar amount of the contract or is a significant change in the protocol (scope of work), a new **R&A Form** will need to be completed. If the amendment deals with other non-monetary issues such as extending the timeline of the study, a new **R&A Form** is not required. Simply fax, email, or send a hard copy of the amendment to OSP for processing.