



Negotiating Clinical Trial Agreements

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Clinical Research

- Clinical: Pertains to or founded on observation and treatment of participants, as distinguished from theoretical or basic science
- Clinical Trial: A research study to answer specific questions about vaccines or new therapies or new ways of using known treatments.
- Clinical trials are used to determine whether new drugs or treatments are safe and effective.
- Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people.



Phases of Clinical Trials

- Phase I – Tests a new drug or treatments in a small group to evaluate its safety, determine a safe dosage range, and identify side effects.
- Phase II – Expands the study to a larger group of people to see if it is effective and to further evaluate its safety
- Phase III – Expands the study to an even larger group of people, monitor side effects, compare it to commonly used treatments
- Phase IV – Takes place after the drug or treatment has been licensed or marketed



Funding of Clinical Trials

- Private (usually pharmaceutical companies)
- State
- Federal
- Federal and private



Clinical Trials at USF

- Pharmaceutical Trials is defined as the testing of a drug or device
- Pharmaceutical testing is subject to the stringent rules and regulations from the FDA
- The management of a clinical trial requires clear and precise procedures for administration



Initiating a Clinical Trial

- Initiating contact between the pharmaceutical firm and the USF faculty can be made by:
- The pharmaceutical company seeking physicians involved in treatment of a specific disease of illness that the drug addresses
- By the physician commonly called a Principal Investigator or PI and/or study coordinator
- The pharmaceutical company sends a copy of the drug study protocol to the PI for review.



Protocol

Protocol:

1. A written document which details the purpose of the study
- 2 Methods and procedures to be followed
- 3 Previous research conducted in the drug or device
- 4 Number of patients to be enrolled
- 5 Statistical, administrative and research reporting requirements, etc.



Successful management of clinical trial requires:

- Protocol approval
- IRB approved informed consent
- Ensure proper communication, translation, and record keeping of informed consent
- Preparing an effective budget and payment schedule
- Negotiating the clinical trial agreement
- Current policies and procedures and Standard Operating Procedures



Steps to negotiating and managing a clinical trial

- PI agrees to the protocol –
(Pharmaceutical study protocols must be followed precisely unless or until the pharmaceutical company amends or modifies the protocol)
- Budget is prepared by the PI, sponsor, with input from DSR
- Agreement is usually issued by the sponsor to the PI and to DSR



Preparing a clinical trial budget

- Budget is generally calculated on a per-patient, per visit or per task basis
- Budget should be simple and should include any additional funds that the pharmaceutical company is granting to USF that are not already included in the per patient basis
- Examples are: equipment, start up, IRB costs, pharmacy set-up, advertising, storage



Clinical Trials budgets (continued)

- Preparing an effective budget can increase compliance and eliminate double billing issues or protect against unreasonable accumulation of residual balance
- An effective budget can ensure that costs are covered either by the sponsor or the patient's/participant's insurer
- Ensure full cost for performing the work
- It should determine which costs are "research only", and which costs are standard of care



Preparing a Clinical Trial Budget (continued)

- Budget should include costs related to adverse events
- Include a contingency for the sponsor to pay for additional tests or procedures that may be needed



Common budget elements

- PI and Coordinator salaries
- Patient procedures
- Supplies
- Equipment
- Other Expenses (phone, fax, shipping, subject payments, records retention, etc.)
- Administrative Cost (IRB Fee, start-up, etc.)
- F&A Costs (Industry recognized rate 27%)



Payment Schedule

- Schedule shows when USF should expect payment for the sponsor. It can be set up as follows:
- Per-patient, per-visit, or per-cost
- Monthly or quarterly lump-sum payments up to the estimated cost of the research project
- A lump-sum fixed price payment made to cover purchases such as equipment with the remaining payments based on a per-patient basis
- The payment plan must differentiate between costs borne by the sponsor and costs borne by other parties

Negotiating Clinical Trials Agreements



- Agreements are usually issued by the sponsor
- A representative from DSR will negotiate the terms and conditions of the agreement as well as the final budget and payment schedule
- Discuss any items in the agreement that appear unclear or unspecific
- Determine if there are specific clauses that relate to the performance of the work that is required by the sponsor
- Discuss proposed budget and payment schedule



Standard Agreement Clauses

- **Effective Dates**
- **Parties** – Sponsor and University – Individuals such as the PI are usually not consider parties
- **Title of the Research** – The sponsors protocol number (agency identification number) and a title of the project should be identified.
- **Object of Research and Research Study Plan:**
 - 1) Physician/PI who will be supervising the research investigation
 - 2) Incorporation of the protocol into the agreement
 - 3) Protections of the faculty and USF from possible non-payment of litigation and/or non-specific results are achieved.



Standard Clauses (continued)

- **Duration of the study.** There are several rules to consider:

The beginning and ending dates chosen in the agreement between USF and the sponsor must be strictly adhered to or a modification of the agreement made

The Physician/PI has the right to terminate the agreement, giving 30 days written notice, if he/she determines that the drug or device is not safe



Standard Clauses (continued)

- **Serious and Unexpected Adverse Event Reports**
- USF must notify its own IRB as well as the Sponsor immediately. USF has policies in place requiring that they communicate any serious events to current or former research participants, as needed
- **Publications.** Publication rights should not be given up. USF will provide a period of time for the sponsor to review the publication
- **Intellectual Property.** Normally intellectual property for clinical trials resides with the Sponsor.



Standard Clauses (continued)

- **Purchasing and Payment.** Usually this is included as an attachment to the agreement
- **Independent Contractor.** This clause protects the Physician/PI and research team from being erroneously assessed federal taxes in connection with payments received from the pharmaceutical company.
- **Complete Agreement.** This clause requires that any and all terms and conditions must be written into the agreement or a modification of the agreement to be legally binding.



Standard Clauses (continued)

- **Governing Law.** As the clinical investigation will be conducted within the State of Florida and subject to the laws of the State of Florida, this clause assures that any litigation or dispute will be settled under these same laws
- **Use of University's Name.** This clause protects the University's name from being used to endorse or advertise any commercial product or material.



Standard Clauses (continued)

- **Modification or Amendment.** This clause requires that all modifications or amendments to the agreement be made in writing and signed by the duly authorized representatives of each party. Modifications or amendments are generally to extend the performance date of the agreement, increase the budget, change the payment schedule, increase the number of patients to be enrolled or evaluation, change performance expectations, etc.



Standard Clauses (continued)

- **Termination.** Termination should be available to both parties. It should be conditional upon certified receipt of a written termination notice and allow the University to receive pro-rated payment for work performed
- **Duly Authorized Representatives.** Individuals authorized to enter into contractual agreements and legally bind their institutions by signing the agreement.
- **Appendix A.** Copy of the Protocol
- **Appendix B.** Budget and Payment Schedule



Establishing a clinical account

- Fully executed agreement
- Protocol
- Budget and payment schedule
- Copy of IRB application and approval
- DSR Proposal and Certification Form (a.k.a. internal form)
- If conflict of interest exists – Financial Relationships Disclosure Form



Monitoring the Study – Post award functions

- PI will receive monthly financial reports on the clinical study
- Reports will show expenditures as well as payments
- PI will send Study Status Log on a monthly basis to the Coordinator of Research Program and Services – USF Health, MDC02



Monitoring the Study – Post award functions

- On-going IRB Approval – During the course of the study the PI must re-apply approval anytime a change is made to the procedures involved in the research, if the investigators change, the IRB approval expires, etc.



Close out of the project

- All final technical and research-related reports are submitted to the pharmaceutical company as required in the protocol.
- A final report must be submitted to the USF IRB and any final reports required by the IRBs at other facilities
- Ensure that all expenses are repaid. Final reconciliation of account is conducted by the USF accounting entity
- A Notice to Close Form and copy of IRB Final Closure Letter is submitted to DSR