NEGOTIATING CLINICAL TRIAL AGREEMENTS WITH FOR-PROFIT DRUG COMPANIES

Presented by

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DEFINITION OF A CLINICAL TRIAL

- Experiment, involving patients, designed to find the most appropriate treatment of future patients with a given medical condition
- Essential characteristic: results from a limited sample of patients are used to determine treatment in the general population

FDA CLINICAL TRIAL PHASES

Testing in Humans				
	Number of Patients	**Length**	**Purpose**	**% of Drugs Successfully Tested**
Phase 1	20 – 100	Several Months	Mainly safety	70%
Phase 2	Up to several hundred	Several months to 2 years	Some short-term safety, but mainly effectiveness	33%
Phase 3	Several hundred to several thousand	1 – 4 years	Safety, effectiveness, dosage	25% – 30%

For example, of 100 drugs for which investigational new drug applications are submitted to FDA, about 70% will successfully complete Phase 1 and go to phase 2; about 33% of the original 100 will complete phase 2 and go to phase 3; about 20-30% of the original 100 will clear phase 3 (and, on average, about 20 of the original 100 will ultimately be approved for marketing).

IMPORTANT ISSUES IN NEGOTIATING THE CLINICAL TRIAL AGREEMENT

[Taken from the Clinical Trials and Tribulations Workshop held at UCLA on March 25, 1998, by Mr. Phil Costic in the Office of Sponsored Research, http://www.ora.med.ucla.edu/issuesclintrial.htm]

- Publication rights
- Confidential information
- Patent rights

(continued)

IMPORTANT ISSUES IN NEGOTIATING THE CLINICAL TRIAL AGREEMENT (2)

- Subject injury
- Payment
- Indemnification
- State law

MONITORING AND QUALITY ASSURANCE

- Protocol compliance
- Data accuracy
- Informed consent
- IRB approval
- Drug accountability

CLINICAL RESEARCH AGREEMENT
CLINICAL STUDY PROTOCOL

- Protocol will be provided by ??
- Protocol will specify:
  - The principal investigator
  - The Study design
  - Information desired
  - Estimated duration of the Study
  - Estimated charges
  - Institution(s) involved

ADDITIONAL PROTOCOL REQUIREMENTS

- Required language for informed consent
- Adverse experiences which must be reported
- Grounds for stopping the study or participation in the study

(continued)

ADDITIONAL PROTOCOL REQUIREMENTS (2)

- Release of patient/subject information to Company, FDA and other governmental agencies
- Medical records and patient privacy
  - *Health Insurance Portability and Accountability Act of 1996 (HIPAA)*

CLINICAL RESEARCH AGREEMENT: Scope Of Work

- Best efforts or completion?
- Phases included (single phase, multiple or options)
- Who is "Investigator"?
- Who provides the IRB, etc.?
- Reporting, data and document management, and treatment responsibilities

CLINICAL RESEARCH AGREEMENT: Term

- Completion or period of time
- Extensions
- Delays
- Force majeure

CLINICAL RESEARCH AGREEMENT: Payment

- Method(s) of payment (e.g. per procedure; per patient; cost reimbursement)
- Time of payment(s)
- Amounts
- Exclusivity of payor (i.e., are multiple sponsors allowed?)

CLINICAL RESEARCH AGREEMENT: Other Cost Issues

- Costs incurred and associated with the diagnosis of an adverse reaction involving the Study Drug
- Costs for treating the adverse reaction
- Other payments (e.g., other compensation from Company if any injury occurs)
- Routine medical care costs
- Referral Fees

CLINICAL RESEARCH AGREEMENT: Principal Investigator

- Can Sponsor approve the Principal Investigator (PI)?
- PI's commitment to conduct the Study
- If the PI becomes unable to complete the Study, must Sponsor consent to a new PI?
- Can Sponsor follow PI?
- Multiple PIs?

CLINICAL RESEARCH AGREEMENT: Records

- Records retention
  - Time for retention
    - Completion or termination of the Study
    - Marketing application approval
    - Discontinuation of the IND
- Maintenance of Study records for the period

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CLINICAL RESEARCH AGREEMENT: Records (2)

- Transfer of Study records
- Ownership of documents
  - *Health Insurance Portability and Accountability Act of 1996 (HIPAA) and State laws on Patient Records*

CLINICAL RESEARCH AGREEMENT: Confidentiality

- Information which is disclosed by Sponsor to the Institution
- Information which is disclosed by Institution to Sponsor
- Third-party information
- Patient/Subject information
- Obligations of Investigator, staff and students

CLINICAL RESEARCH AGREEMENT: Promotional Activities

- Use of name of Sponsor/Institution
- Use of PI's name
- Trademarks
- Publicity
- Advertisement for patients
- Press releases
- Inquiries from media and financial analysts

CLINICAL RESEARCH AGREEMENT: Publications and Scientific Communications

- Right to publish the results of the Study
- Other rights to discuss Study (e.g. conferences – where and when)
- Notification to Sponsor
  - Prior to submission

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CLINICAL RESEARCH AGREEMENT: Publications and Scientific Communications (2)

- Notice if publication contains patent information
- Right to delay
- Nonscientific journals, newspapers, radio or television

CLINICAL RESEARCH AGREEMENT: Intellectual Property Rights

- Inventions
  - Ownership
  - Licensing
  - Joint inventions
- Data
  - Copyright
  - Databases

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CLINICAL RESEARCH AGREEMENT: Intellectual Property Rights (2)

- Administration of Intellectual Property
- Biological materials

CLINICAL RESEARCH AGREEMENT: Indemnification

- Who indemnifies and who is indemnified?
- From what?
- Expenses of claims and suits related to what injuries?
- Caused by – IN WHOLE OR IN PART?
- By any substance studied or any procedure performed in accordance with the provisions of the protocol

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CLINICAL RESEARCH AGREEMENT: Indemnification (2)

And

- For use by Sponsor of the results of the Study
- Product liability
- Indemnification without prior payment by Institution

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CLINICAL RESEARCH AGREEMENT: Indemnification (3)

- Exclusions from obligation to indemnify
  - Failure of the Institution to comply with any applicable governmental requirements or to adhere to the terms of the protocol?
  - Negligence of the Institution, officers, agent or employee, subcontractors?
- Some states will not allow indemnification of negligence or failure to comply with law

CLINICAL RESEARCH AGREEMENT: Conditions to Indemnification

- Notice of any claim or lawsuit
  - Right to defend the lawsuit
    - Subject to Institution's right to retain the counsel of its choice?
- Right to settle the claim
- Right to require the indemnified party to cooperate fully in the investigation and with defense of any such claim or lawsuit

CLINICAL RESEARCH AGREEMENT: Additional Indemnification Issues

- Costs of extra unanticipated tests, treatments, and hospitalizations of patients required as a result of adverse events
- Costs covered by the subject's or patient's medical or hospital insurance or by governmental programs providing such coverage

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CLINICAL RESEARCH AGREEMENT: Additional Indemnification Issues (2)

- Non-medical indemnification (e.g., worker's compensation, third-party injuries, public health costs)
- Insurance

CLINICAL RESEARCH AGREEMENT: Compliance with Law

- Debarment Certification (FDA certification)
- Conflict of interest
- Integrity in science
- Misconduct
- UBIT
- State laws
- Foreign countries

CLINICAL RESEARCH AGREEMENT: Additional Topics

- Independent contractor status
  - Should Institution ever act as Joint Venturer?
- Notices
  - To whom, where, and for what?
- Modifications and amendments
  - Who has the right to require, when, and what if required by Government or science?

CLINICAL RESEARCH AGREEMENT: Inspections and Access

- May Sponsor inspect Institution's procedures, facilities and Study records?
  - May information obtained from such inspections be shared?
  - With whom and for what purposes?
- Access to patients, records, data, faculty, treatment facility, etc.

CLINICAL RESEARCH AGREEMENT: Study Drug/Device

- For what purpose(s) may Drugs furnished for Study ("Study Drugs") be used?
- When and how is Study Drug provided?
- Storage and accounting for Drug
  - DEA registration
- Derivative compounds, by-products and waste disposal

CLINICAL RESEARCH AGREEMENT: Disputes

- Method(s) of dispute resolution
- Costs and attorney's fees
- Jurisdiction and venue
- Right to jury
- Subcontractor disputes

CLINICAL RESEARCH AGREEMENT: Termination

- Reasons for termination
- Payment on termination
- Responsibility for patients/subjects on termination
- Students and other personnel
- Close-out

CLINICAL RESEARCH AGREEMENT: Additional Sources of Information

- http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm129515.pdf
  - Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance
- www.clinicaltrials.gov
- www.fda.gov/cder/about/whatwedo/testtube.pdf (FROM TEST TUBE TO PATIENT:IMPROVING HEALTH THROUGH HUMAN DRUGS)
- www.utsystem.edu/OGC/ University of Texas Office of General Counsel
- www.fda.gov/oc/oha/default.htm#clinical Food & Drug Administration Clinical Trials site
- www.aamc.org/advocacy/issues/research/start.htm Association of American Medical Colleges site

QUESTIONS AND ANSWERS