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**Negotiating Clinical Trial Agreements: Balancing the Interests of Sponsors and Healthcare Providers**

Structuring Indemnification, IP Rights, Confidentiality and Other Key Provisions

**THURSDAY, MAY 5, 2016**

1pm Eastern | 12pm Central | 11am Mountain | 10am Pacific

Today’s faculty features:

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CLINICAL TRIAL AGREEMENTS

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Goals and Topics

• Discuss the importance to clinical trials of a solid CTA
• Discuss some key issues in negotiating and drafting CTAs
• Cover a variety of research contract issues, ranging from baseline issues to current challenges
AGENDA

• Background
• Research-Related Injury Issues
• Compensation
• Subject Enrollment
• Indemnification and Insurance
• Access to and Use of Study Data
• Intellectual Property Issues
• Publication
• Confidentiality Issues
• Conclusion
BACKGROUND
Definitions

• What is “research”?
  – 45 CFR 46.102(d): “systematic investigation...designed to develop or contribute to generalizable knowledge” about human disease and healthcare.

• What is a clinical trial?
  – Research involving humans as subjects who receive specific interventions according to the research plan or protocol created by the investigators.
Common Purpose, but Competing Perspectives

- All parties to a clinical trial have a common purpose of conducting a successful trial.
- But the parties have competing perspectives.
  - Sponsor Perspective
  - Site/Institution Perspective
  - Other Perspectives
Steps for Initiating the Clinical Trial

• Site Identification
• Recruitment Plan
• Confidentiality/Non-Disclosure Agreement
• Trial Documents
  — Protocol
  — Informed Consent
• IRB Approval
• Clinical Trial Agreement
• CTA: Who, what, where, when, why?
  – Tells you parties, subject matter, involved sites, the term, and the purposes/intent of the parties
  – Includes responsibilities, rights
Who will be involved in the CTA, and how will they be involved?

• Type of Study
  – Sponsor-initiated vs. Investigator-initiated is important factor

• Parties to the CTA
  – Sponsor, site, PI(?), subcontractors(?), CRO(?)
  – Consider potential for changes over time (e.g. PI movement)
  – Special considerations if PI is not employed by the site (e.g. private practice physician)
What Should the CTA Address?

- Obligations of the parties
- Compliance
- Risk/Liability
- Rights and protections: IP issues; Confidentiality; Publication; Handling of Study Data; etc.
- Payment
- Term and Termination
- “What-ifs”
RESEARCH – RELATED INJURY ISSUES
Payment for Research – Related Injury/Illness Treatment Costs

• Ethical and Practical Issues
  • Research principles in the Belmont Report* support providing compensation
    • Respect for Persons
    • Beneficence (minimize harms and maximize benefits)
    • Justice (fair distribution of research benefits and burdens)

• Practical problems:
  • Financial consequences for research sites and sponsors
  • Determining causation of injury
    • “Substantial factor” test?
    • Use independent individual to determine causation?
    • Appeals process?
  • Identifying compensable “harms”
    • Emotional harm?
    • Long term care?
    • Pain and suffering? Lost wages? Punitive damages?
    • Monetary cap?
  • Exclude any of the following?
    • Pre-existing conditions
    • MD negligence, reckless misconduct
    • Institutional negligence, reckless misconduct
    • Injuries sustained by subjects who don’t follow instructions
Legal Issues

For research involving more than minimal risk, federal regulations do require discussion regarding availability of compensation and treatments for research-related injuries; federal regulations do not require researchers, sponsors or research sites to offer payment for treatment of injuries. 45 CFR 46.116; 21 CFR 50.25
Medicare Secondary Payer Issues

- In general, Medicare is secondary to other insurers.
- Does sponsor’s “promise to pay” for study-related injuries if insurance doesn’t cover make sponsor a primary payer?
- 2004 CMS letter regarding application of MSP to clinical trial injury coverage in situation where sponsor agreed to pay for medically necessary services related to injuries resulting from research participation if these services were not otherwise covered by another payer.

- The clinical trial sponsor’s agreement with trial participants that it will pay for medically necessary services related to injuries participants may receive as a result of participation in the trial constitutes a plan or policy of insurance under which payment can reasonably be expected to be made in the event such an injury occurs...Therefore, Medicare will not make payment if it is aware [of such a situation.]

As of July 1, 2009, Section 111 (8) requires liability insurance plans to take these steps when claim is filed against a plan or against an individual or entity insured or covered by the plan:

- Identify whether claimant is Medicare beneficiary
- If claimant is identified as Medicare beneficiary, report to CMS the identity of the beneficiary and other specified information required to enable coordination of benefits determination

May 26, 2010 CMS “Alert” reiterated that sponsor’s payments for research-related injury treatment costs must be reported pursuant to Section 111 of MMSEA

Do above requirements raise HIPPA concerns?

Note: unlikely that sponsor could shift reporting requirements to site in CTA
Practices

• Variability in CTAs regarding sponsor coverage in terms of:
  • Payment to subject vs. reimbursement to Institution for treating subject’s injury
  • Payment for only emergency treatment
  • Payment of Institution’s costs vs. fees
  • Payment secondary to private insurance coverage

• Fairness concerns when sponsors allowed to bill private insurers primary to sponsor coverage
  • Imposes costs on subjects in form of co-payments, deductibles, increased premiums
  • Such costs may make participation financially impossible for some, creating bias against privately insured subjects (compared to Medicare beneficiaries and uninsured, who are not required to pay these costs)
COMPENSATION
• CTA specifies what, how and when Site will be compensated; how IRB/EC will be paid; how payment will be accounted for and discrepancies will be resolved.
  
  o Issues, Concerns:
    – To avoid Anti-Kickback concerns, assure fair market value exchange
    – Regarding payments for start-up costs, assure clarity in what’s covered, consider whether certain payments for start-up costs should be non-refundable regardless of whether Site participates in Study.
    – Hold-backs can create cash flow problem for Site
    – Charge interest for late payments from Sponsor?
    – Sponsor may not wish to pay for Study activities prior to termination if Agreement is terminated due to Site breach
SUBJECT ENROLLMENT
CTA may specify timing of subject enrollment, enrollment goal, enrollment limitations

- Issues, Concerns:
  - Sponsors generally desire rapid enrollment - but need to comply with inclusion/exclusion criteria
  - Ensure timing requirements are feasible for institution - e.g., enroll first subject within 60 days of receiving IRB approval
  - Ensure language does not encourage PI to coerce potential subjects
  - Best efforts to enroll v. reasonable efforts to enroll
INDEMNIFICATION AND INSURANCE
• Indemnification
  o Sponsor often indemnifies Site Indemnitees with exceptions (including if potential liability was caused by Site’s negligence).
  o Site often objects to assuming indemnification obligations; insurance may not cover cost of defending Sponsor
• **Insurance**
  
  o Site often represents that it carries specified general liability and malpractice insurance and that insurance covers the Study; Sponsor often represents that it carries general liability and product liability insurance and that insurance covers the Study.
  
  o **Concerns:**
    
    – Sponsor’s product liability insurance may not include clinical trial coverage
    
    – Site’s malpractice insurance may not include clinical trial coverage
    
    – Request certificate of insurance or self-insurance information to confirm
ACCESS TO AND USE OF STUDY DATA
• Sponsor may desire to use study data for any purpose - future research, development, and marketing
• Ensure consistency between CTA language and informed consent/HIPAA authorization from
• Address sponsor’s access to Institution’s source documents
INTELLECTUAL PROPERTY ISSUES
Intellectual property access and ownership

• An IP assessment
  • Whose IP is being used for what
  • What IP could potentially be created (Likelihood of invention may depend on phase of trial or type of research)
What the CTA should address?

• Definition/Scope
• Disclosure
• Publication
• Ownership
Definition/Scope

- What is Intellectual Property?
  - Patents
  - Copyright
  - Trademarks
  - Trade Secrets

- Existing IP
Disclosure and Publication

- Internal vs. External Disclosure

- First to File - priority given to first applicant to file for protection of an idea, not to first to invent
Ownership Issues

• Sponsor-Initiated Trial
  – Sponsor’s position: Sponsor owns all inventions arising from study; we’re paying; it’s our protocol and our product
  – Site’s Response:
    o Trial conducted by our researchers and at our facilities
    o Discoveries are an objective of our institution. As part of our obligation to society, we need to communicate discoveries to the public.
    o For our researchers, it’s “publish or perish.”
Ownership Issues

• Investigator-Initiated Trial
  - Sponsor’s position: Sponsor owns all inventions arising from the study; we’re paying and (maybe) providing product
  - Site’s Response:
    o Site PI wrote the protocol
Potential Compromises

• Compromises:
  o Sponsor owns all, with site receiving free non-exclusive license for non-commercial purposes
  o Site owns all, with Sponsor receiving non-exclusive license and option to negotiate exclusive license
  o Site owns all, with Sponsor automatically receiving an exclusive license
Sponsor’s goals, concerns

- **Overall goals:**
  - Generate data, properly complete the study
  - Obtain marketing approval
  - Protect IP via patents

- **Publication goals:**
  - Validate scientific basis for intervention
  - Information for investment community
Institution’s goals, concerns

• Free scholarly exchange (good and bad results) and the expansion of ideas
• Scholarly publication, professional development
• Advance science and improve public health
• Generate IP and new avenues for research
• Compliance with registration requirements
• Maintenance of tax exempt status
Variations in CTA

- Type of publications allowed, addressed (articles in peer reviewed journal, abstract submissions, posters, oral presentations, posting to www.clinicaltrials.gov)
- Sponsor review times (e.g., expedited times for poster presentations and abstracts)
- Restrictions to publishing (e.g., sponsor right to request deletion of Sponsor confidential information, not results; additional delay 40-60 days to protect IP/file patent application)
CONFIDENTIALITY ISSUES
Competing Perspectives

- Sponsor Perspective
- Site Perspective
Potential Hurdles

- Defining the scope
- Informing the key players
- CI that is already public
What the CTA should address?

- Practical and decipherable definition
- Checks and Protections
- Exemptions
Definition

- Agreement and Exhibits
- Study Data
- Other proprietary information
  - To mark or not to mark
Checks and Protections

• Separate acknowledgement

• Injunctive relief

• Destruction upon termination

• Term of obligation
Exemptions

• Subpoena or Court Order

• Public information

• Prior possession

• Independently determined/discovered

• Necessary to disclose for medical care of a study subject
CONCLUSION