Overview of Clinical Trial Agreements

ACCR – October 18, 2019

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Overview

• Office for Sponsored Research
• Different Missions
• What is this Document?
• Clinical Trial Agreement (CTA) Walk-Through
• Brief Overview: CTA Process
• Review: Key Points
• Questions
Office for Sponsored Research

• Central university office

• Responsible for:
  – Negotiating sponsored research agreements (funded and non-funded)
  – External funding and non-funded agreements (but usually internally-funded projects)
  – Reviewing, submitting and accepting federal and foundation grants and awards
  – Signing research-related contracts on behalf of institution

• Works with other university units:
  – INVO (tech transfer), COI Office, IRB, IACUC, NMHC, General Counsel, ASRSP (accounting services for research), and others, as needed
  – Facilitates coordination where needed
Different Missions: Industry and AMC

• Different Missions
  – Universities and for-profit corporations have many incompatible purposes, objectives, and philosophies.
  – **The challenge**: Support the mission of each partner within the constraints that limit each partner.
  – University / Academic Medical Centers (AMC): Treat patients, create and disseminate knowledge, and educate.
  – Companies: Profitability, responsibility to shareholders, bring new and better products to market.
<table>
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<th>Agreement Type</th>
<th>Description</th>
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What is a CTA?

• CTA = Clinical Trial Agreement
  – Binding contract
  – Usually between university or AMC and corporation
  – Establishes:
    • Payment terms
    • Agreed-upon regulatory framework
    • Liability allocation
    • Responsibilities
    • What happens before, during, and after the trial
CTA: Walk-Through

- Key Sections
  - Preamble and Scope of Agreement
  - Confidentiality
  - Data Use & Privacy
  - Publication
  - Study Monitoring & Auditing
  - Indemnification, Liability, and Insurance
  - Subject Injury
  - Representations & Warranties
  - Inventions
CTA: Preamble and Scope

• Preamble:
  – Background (underlying facts)
  – “Whereas” clauses (why)
  – Recitals (relevant information; objectives; common understandings)
  – Related Agreements

• Scope
  – Not always in contracts; common in master agreements
CTA: Confidentiality

• What it does:
  – Defines what is “Confidential Information.”
  – Indicates what specific uses of CI are allowed.
  – Describes exceptions to CI.

• Why have it:
  – Protects proprietary information from unwanted disclosure.
  – Usually replaces or overrides earlier confidentiality agreements.

• Time-limited
• Unilateral or bilateral

• Note: Trade Secrets – sharing generally avoided in academic research
Sample:

- "Confidential Information" refers to information of any kind which is disclosed to the Institution by Sponsor for purposes of conducting the Study or Data (as defined below) which: (i) by appropriate marking, is identified as confidential and proprietary at the time of disclosure; (ii) if disclosed orally, is identified in writing within thirty (30) days as being confidential; or (iii) is of such a nature that a reasonable person familiar with the Study would consider it to be confidential or proprietary from the context or circumstances of disclosure.

- NOTE: Usually research institutions either remove “data” or carve out “data” for publication and presentation purposes.
CTA: Confidentiality

• Problem areas:
  – Defining what is confidential
  – Survival
    • Academic Medical Centers (AMCs) prefer shorter survival
    • Industry prefers longer or indefinite
  – Exceptions
    • Medical records/physician’s notes
    • Publicly available, already in possession, independently developed, provided by third party, and court/administrative-ordered disclosures
CTA: Data Use & Privacy

• Why Have Data Use Section?
  – Allows parties to understand what is “data” and what they can do with it (and can’t do with it).

• What it does:
  – Defines what Data is and is not
  – Limits uses of data for each party
    • Only for the specific research project?
    • Commercialization, as needed?
    • Future internal uses?
    • Sharing? See confidentiality section, as well.
  – Most universities require right for internal, non-commercial use and use in publications; most sponsors require use for commercialization.
CTA: Data Use & Privacy

• Data Use Sample:

  “Data” shall mean all data and information generated by Institution as a result of conducting the Study in accordance with the IRB approved Protocol. Data does not include original Study subject or patient medical records, research notebooks, source documents or other routine internal documents kept in the Institution’s ordinary course of business operations, which shall remain the sole and exclusive property of the Institution or medical provider. Sponsor shall own and have the right to use the Data in accordance with the signed Informed Consent and authorization form, applicable laws, and the terms of this Agreement. Notwithstanding any licenses or other rights granted to Sponsor herein, but in accordance with the confidentiality and publication sections herein, Institution shall retain the right to use the Data and results for its publication, IRB, regulatory, legal, clinical, educational, and internal research purposes.
• Privacy:
  – Note: Corporate sponsors are generally not covered entities.
  – Health Insurance Portability and Accountability Act of 1996 and its implementing regulations (HIPAA) – acknowledge each party’s responsibilities.
  – If sponsor does come in contact with any protected health information (PHI), sponsor is asked to use reasonable safeguards for the protection of such PHI.
  – Any use or storage of such PHI must be consistent with what was agreed to within the informed consent document/HIPAA authorization form.
CTA: Publication

• Why is this in the CTA?
  – Most universities and AMCs require publication rights
  – Non-profit institutions: mission to disseminate information and educate (tax exempt status → need for societal benefit)

• What it does:
  – Outlines what can be published and when
  – Allow for reasonable delay for review/comment—but never approval—and for patent applications
CTA: Publication

• **Sponsor’s concerns:**
  – Accuracy of reporting.
  – Protecting confidential and proprietary information.
  – For multi-center studies, allowing for a complete publication that incorporates results from all sites.

• **Compromise:**
  – AMC will allow sponsor to “review and comment” and consider those comments in good faith.
  – AMC will agree to delay publication for reasonable period after the study is completed (for multi-center studies).
• **Sample:**

Institution shall be free to publish, present or use any Data and results arising out of the Study (individually, a “Publication”). At least thirty (30) days prior to submission for Publication, Institution shall submit to Sponsor for **review and comment** any proposed oral or written Publication ("Review Period"). Institution will **consider any such comments in good faith** but is under no obligation to incorporate Sponsor’s suggestions. If, during the Review Period, Sponsor notifies Institution in writing that: (i) it desires patent applications to be filed . . . Institution will **defer Publication for a period not to exceed sixty (60) days, to permit Sponsor to file any desired patent applications**; and (ii) if the publication contains Sponsor’s Confidential Information . . . the Institution agrees upon Sponsor’s written request to delete such Sponsor’s Confidential Information (other than Study Data or results).

• **NOTE:** First publication will be limited to multi-center publication (for multi-center studies); otherwise, site is usually free to publish its own results after that or within 1-2 years following completion of the study.
CTA: Study Monitoring & Auditing

• Why is this in the CTA?
  – Sponsors have duty to monitor and audit many studies;
  – Sites have responsibility to actively participate.

• What it does:
  – Outlines parameters for monitoring and auditing by sponsor and the FDA.
    • Usually, scheduled in advance at mutually-agreeable times.
    • Limits on what a sponsor can access at the study site?
  – Establishes protocol outline for response to audits by sites.
    • Notification of sponsor when FDA indicates it will audit.
    • Sponsor participation in AMC’s response to FDA inspection?
  – Who pays for this time?
CTA: Study Monitoring and Auditing

Sample:

- Site visits by Sponsor and/or its authorized designee will be scheduled in advance for times mutually acceptable to the Parties during normal business hours. Sponsor’s . . . access is subject to reasonable safeguards to ensure confidentiality of medical records and systems.

- Upon becoming aware of an audit or investigation by a regulatory agency . . . Institution agrees to provide Sponsor with prompt notice of the audit or investigation. Sponsor may be available or request to be present with approval from auditor during such audit, but Sponsor agrees not to alter or interfere with any documentation or practice of Institution. Institution shall be free to respond to any regulatory agency inquiries and will provide Sponsor with a copy of any formal response or documentation to the regulatory agency regarding the Study.
CTA: Indemnification, Liability, and Insurance

• Why is this in the CTA?
  – Both parties want to minimize risk and it is useful to appreciate what risks you are taking on when conducting or sponsoring a study.

• What it does:
  – Language whereby one party agrees to protect another against an anticipated loss or damage arising out of the trial.
  – Sponsor-initiated studies:
    • Sponsor should indemnify AMC against and insure for any loss or damage incurred as a result of conducting the study
      – Sponsor’s use of the study data/results
      – Third-party claims
      – Sponsor’s negligence or misconduct
  – Investigator-initiated studies:
    • Each party normally indemnifies the other against any loss or damage the results from the indemnifying party’s negligence or misconduct.
CTA: Indemnification, Liability, and Insurance

• Most AMCs:
  – Have strict insurance requirements in all sponsor-initiated clinical trials
    • In the event a sponsor is unable to meet these requirements, the study may undergo a clinical/financial risk assessment
    – Party who stands to gain most financially should bear most risk, taking into account other considerations, such as for-profit or non-profit status and so on.

• Both parties want to:
  – Minimize costs and avoid risks
CTA: Indemnification, Liability, and Insurance

• Sample:
• Sponsor agrees to **defend, indemnify, and hold harmless** the Institution and its medical affiliates and affiliated hospitals, and each of their trustees, officers, directors, governing bodies, subsidiaries, affiliates, investigators, employees, IRB members, agents, successors, heirs and assigns (collectively referred to as "Institution’s Indemnitees"), from and against any third party claims, loss, damage, cost and expense of claims (including reasonable attorney’s fees) and suits **to the extent** caused by or arising from the **proper conduct of the Study** or **proper use of the Study Drug or Study Device** under this Agreement or from the **use of the Study results** ("Claims"), regardless of the legal theory asserted.
CTA: Indemnification, Liability, and Insurance

- **Indemnify**: Mechanism to shift risk from one party to another.

- **Defend**: Duty to defend another party against third party claims.

- **Hold Harmless**: Bars one party from bringing an action against the other.
CTA: Subject Injury

• Why is this in the CTA?
  – Subject injury protection is important to AMCs and study subjects in clinical trials – often required by AMC policy.

• What it does/how it works:
  – NOTE: No U.S. federal law requires subject injury compensation.
  – Near-term mechanism for reimbursement of treatment costs related to illness or injuries.
  – CTA and Informed Consent language should be consistent, not the same.
  – Billing language, if present, should be carefully phrased to avoid secondary-payor and other issues.
  – This is another “cost of doing business” related to sponsor-initiated clinical trials.
CTA: Subject Injury

• Sample:
• If a Study subject suffers an adverse reaction, illness or injury which, in the reasonable judgment of Institution and Sponsor, was directly caused by a Study Drug or Study Device or any properly performed procedures required by the Protocol, Sponsor shall reimburse for the reasonable and necessary costs of diagnosis and treatment of any Study subject injury, including hospitalization, but only to the extent such expenses are not attributable to (i) Institution's negligence or willful misconduct or (ii) the natural progression of an underlying or pre-existing condition or events, unless exacerbated by participating in the Study.

  — NOTE: Many, if not most AMCs require that sponsors agree to pay for medically necessary services related to injuries study subjects may receive as a result of participation in the trial and cannot agree to first seek reimbursement from Medicare or commercial insurers.
CTA: Representations & Warranties

• Why is this in the CTA?
  – The parties want to set specific expectations or conditions.
  – Usually, in relation to debarment and exclusion only.

• What does it do?
  – Demonstrates key facts or requirements that one or both parties rely on in entering into the Agreement.
  – Establishes guarantee or warranty (or lack thereof).
    • NOTE: AMCs typically do not warrant their research data or results.
    • NOTE: Failure of certain representations, certifications, or warranties may mean a party is in breach or the contract may be voidable.
CTA: Representations & Warranties

• Sample:
  • The Institution represents that to its knowledge neither it, nor any of its employees, agents or other persons performing the Study under its direction, is currently **debarred, suspended or excluded** under the Federal Food, Drug and Cosmetic Act, as amended, or disqualified under the provisions of 21 CFR § 312.70. In the event that the Principal Investigator or any Study personnel becomes debarred or disqualified during the term of this Agreement or within 1 year after termination of the Study, the **Institution agrees to promptly notify Sponsor after learning of such event**. Institution certifies that it is not excluded from a federal health care program including Medicare and Medicaid. In the event an Institution becomes excluded during the term of this Agreement or within 1 year after termination of the Study, the Institution agrees to promptly notify Sponsor after learning of such event.
CTA: Inventions

• Why is this in the CTA?
  – Each party wants to protect its intellectual property.

• What does it do?
  – Apportions rights to inventions that might arise out of the study.
  – Allows parties to protect their respective investments.

• NOTE: Sponsor-initiated or investigator-initiated?
CTA: Inventions

• Sponsor-Initiated
  – *Company* typically has pre-existing IP rights, including patents on the Study compound or device
  – *AMC* prefers to retain ownership of new uses for the compound/device not anticipated by Protocol (unlikely)
    • however, typically gives sponsor a time-limited option for an exclusive license with a royalty rate

• Investigator-Initiated
  – *AMC* IP is embedded in the Investigator-written protocol
    • But, use of funder’s proprietary product may diminish invention rights of *AMC*
CTA Process

• Negotiation by sponsored research / contracts office or general counsel
  – May involve Contract Research Organization (CRO)
  – Back and forth on terms involves email and phone calls
  – Sign-offs needed?
    • Regulatory Compliance
    • Patent Attorney
    • Conflict of Interest
    • Risk Management

• Budget negotiation is responsibility of department at NU.
Model and Master CTAs

• Master CTAs:
  – Single Agreement intended to cover multiple trials
  – Usually a 5-7 year term
  – Each study agreement is reduced to a “Work Order” or Exhibit to the Master CTA

• Accelerated Clinical Trial Agreement (ACTA):  https://www.ara4us.org/

• MAGI Model CTA:  https://magiworld.org/standards/
Review

• Differing missions explain areas of contention
• What’s in the CTA matters to the work people do on a study:
  – Preamble and Scope of Agreement
  – Confidentiality
  – Data Use & Privacy
  – Publication
  – Study Monitoring & Auditing
  – Indemnification, Liability, and Insurance
  – Subject Injury
  – Representations & Warranties
  – Inventions
Review (continued)

• Negotiation takes time:
  – Liability
  – Publication rights
  – Rights to data (what about after the study is over)
  – Research subject protections
  – Policy and Laws:
    • Corporate, institutional, federal, state, local, and international laws, regulations, and guidelines.
  – Two parties, but multiple individuals working to finalize acceptable terms.
Questions?

Thank you!
Sources / Contact Information

- Sources include: UIDP (University Industry Demonstration Partnership) and the workgroup for the Accelerated Clinical Trial Agreement (ACTA), under the Clinical and Translational Science Awards Consortium Steering Committee (https://www.ara4us.org/).

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