SELECTED EXCERPTS FROM

"Intellectual Property Provisions in Clinical Trial Agreements"

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Presentation Overview

- General Introduction
- Introduction to Intellectual Property
  - Copyrights
  - Trademarks
  - Trade Secrets
- Patents and Inventions
- Study Data and Confidentiality
- Biospecimens (and Informed Consent)
- Wrap-Up and Questions

Sponsor Overall Perspective on Clinical Trials

- Estimated cost of a New Drug—Phase 1 to market: $1 Billion+
- This is more than double cost in 1980's and 5x cost in 1970's
- Cost increases largely driven by clinical trials
- This includes major increases in FDA required post-approval commitments
- Huge financial investment – needed to fund pre-clinical development, clinical development (phases 1 through 4) and commercialization of the Drug.

Institution Overall Perspective on Clinical Trials

- Mission critical for advancing patient healthcare
- Internal IP Policies
- Federal considerations under the Bayh-Dole Act
- Investigator interest and Career Development
- Tax-exempt Scientific Research and Tax Exempt Bonds used to finance facilities
  - Applies to all educational, scientific, non-profit corporations under 26 U.S.C. paragraph 501 (c)(3)
  - Study MUST be conducted in the PUBLIC INTEREST and carried on in furtherance of the purpose for which Institution was granted its exempt status:
    - performed for the benefit of public or aiding community
    - results available to public without unreasonable restrictions/delay
    - enhance level of care and treatment options for patients
    - enhance knowledge of clinical staff
    - aid scientific education of Institution's students or residents
    - No works for hire that could be considered business use.

Type of Clinical Trial Affects Many Issues

- Sponsor-Initiated Clinical Trials
  - Sponsor's protocol, drug and Sponsor holds the IND
  - Sponsor likely using data to support FDA application
  - Sponsor provides full funding and study drug, direction on conduct of trial
  - Institution/Investigator less "creative" in the conduct of the study
- Investigator-Initiated Clinical Trials
  - Investigator's protocol and Investigator holds IND (IDE)
  - Sponsor provides limited funding and study drug
  - Sponsor significantly less "directive" in the conduct of the study
  - Sponsor still needs access to certain data (such as adverse event data)

One Way to Categorize IP in Clinical Trial Agreements: 3 Types

- **Background Intellectual Property** – developed PRIOR to the Study by either party.
- **Study Intellectual Property** – developed DURING performance of the Study by one party.
- **Joint Study Intellectual Property** – developed DURING performance of the Study by BOTH parties.

Other Ways to Categorize IP in Clinical Trial Agreements:

- Who funds creation of the IP?
- Does compound arise from the drug/device?
- Who needs exclusive rights / ownership of the IP?
  - For what purpose(s)?
- Who needs non-exclusive license to use the IP?
  - For what purpose(s)?

Patents - General

- Protects a new and useful process, machine, or composition of matter, method of use, i.e., an invention
  - "Anything made by man"
- The right to prevent others from making, using, selling, offering to sale or importing invention.
- An application to the government is necessary (not automatic)
- Term of patent: 20 years from filing application (but extensions possible for prosecutorial delays under A.I.A.)
- BIG CHANGE – A.I.A. – "First to File" instead of "First to Invent"
- Biosimilars – everything still up in the air

What is Patentable?

- To be patentable, an invention must have all of these qualities:
  - Novel
  - Useful
  - Non-obvious
  - and, both conceived and reduced to practice (i.e., proven to work)
- CRITICAL: Cannot patent if already published or in public use. This is an absolute bar to patent protection throughout the world. A single public disclosure not under an obligation of confidentiality counts! (Need to cover inadvertent disclosures in CTAs/CDAs.)
  - Must contain desire to "share science with the world"
  - Note: The prior 1 year grace period in U.S. has been modified (but not totally eliminated) by the A.I.A.
- For a summary of A.I.A.'s major changes:
  - http://ratnerprestia.com/264

Potential Inventions Resulting from Clinical Trials

- New uses of the study drug (e.g. Viagra)
- Identification of biomarkers of the drug or disease
- Methods of administration
- Dosing regimens
- Drug combinations
- New inventions that relate to the Protocol but not specifically to the Study Drug (ex: new diagnostic, end point)

Most Famous (and Valuable) Side Effect in History

- In 1989, Pfizer synthesized sildenafil citrate and named it UK-92,480.
- Preclinical testing indicated potential as a treatment for angina pectoris.
- Clinical trials started in 1992, with negative results.
- An investigator mentioned that, at a dose of 50 mg, side effects appeared, including indigestion, backache and penile erection.
- The FDA approved UK-92,480 at 50mg dose, now known as Viagra, in 1998.
- In 2008, Pfizer's Viagra generated ~1.93 billion U.S. dollars of revenue (Source: Statista).

N.Goldfarb, Journal of Clinical Research Best Practices. Vol. 2, No. 3, March 2006

Inventions: Sponsor Perspective

- When inventions are valuable, they can be *really* valuable
  - Holding IP rights central to incentivizing investment in innovation
  - Strong and predictable patents are critical. Some drug compounds can be protected by only 1-2 patents
  - Market exclusivity important to offset R&D costs
    - A single successful drug costs over $500M to develop (not counting the costs of failed candidates along the way). Protect investment & offset failures.
  - $ success = ability for global access, patient support programs
- Sponsor concerns:
  - The Institution demanding unreasonably high fees or royalties
  - The Institution having other IP that is required to use or practice the invention, and declining to license it ("blocking"). At minimum, NERF!
  - Investing in upfront fees and royalties for an early stage invention, only to find out it was not really so great

Inventions: Institution Perspective

- Why do institutions do tech transfer?
  - Public benefit. IP protection gives the companies the protection they need to justify investing millions in developing a commercial product from early stage academic research.
  - Economic Development. Start -ups provide good quality regional jobs.
  - See practical applications arise from lab research; improve quality of life.
  - Federal law (Bayh-Dole Act) requires that results from federally funded research be developed to benefit taxpayers.
  - Attract and retain top faculty.
  - Revenues (shared with inventors/creators).
  - Economic Development – startup companies may provide high-quality jobs.
  - Generates income to promote and support teaching and research.

Key Patent Negotiation Issues

- Scope / apportionment of inventions
- Ownership vs. use rights
- License grants
  - non-exclusive
  - exclusive
  - research use only
  - commercial use
  - field limitations
- Option rights – exercisable for licenses, whether on pre-specified terms or TBD terms

Sponsor-Initiated CTAs: Sponsor Perspective on Ownership of Inventions

- How will Institution invent something in an industry-sponsored trial under an industry protocol?
  - "But for" Sponsor's protocol, the Institution would have nothing.
  - Institution must implement study exactly in accordance with protocol: how can there be a new therapy?
  - Institution must only use study drug in accordance with protocol: how can there be a new use or dosing regimen?
- Sponsor is fully funding the Study! And providing the study drug!
- Sponsor should own all inventions

Sponsor-Initiated CTAs: Institution Perspective

- Institution is providing valuable knowledge and skills in the performance of the clinical trial, and Institution's research efforts involve hundreds of projects with many difference sponsors: more than just the one Sponsor Study.
- Reasonable to agree to assignment for a narrow scope:
  - Patentable inventions only;
  - Conceived and reduced to practice "directly in the performance of the Protocol" (vs. broader "arising from" or "resulting from"); and
  - Directly related to study drug, its analogs, derivatives, etc.
- Exclude all background technology/inventions of Institution
  - Not funded by sponsor
  - May not have been created by the study PI
  - May already be encumbered
  - Grant of non-exclusive license would make it impossible to otherwise commercialize.

Negotiation Tips and Potential Compromises

- Limit ownership to inventions which directly [relate to] [are either a method of use or composition of matter of] [incorporate] the Study Drug and made by PI and study team.
- Institution must retain some rights for [educational] [internal non-commercial] purposes
- If Institution retains rights to "other" inventions, Sponsor should be sure to get at least a non-exclusive license with an option for an exclusive license
- Consider an option or right of first refusal
- Consider patent prosecution responsibility: who controls, who pays, cooperation & communication
- State institutions may not be able to assign any inventions under state law.
- Tax-exempt status must be protected. Cannot assign everything.

Inventions in Investigator-Initiated CTA: Institution Perspective

- Scope of inventions should be similar to Sponsor-initiated CTA
- Standard IP policies of the University should apply
- Sponsor provided an option to negotiate for an exclusive license to Inventions.
- Sponsor may have a right to a non-exclusive, royalty-free license to use Inventions for internal research purposes.
- Institution should be compensated if creating or increasing value of a company's drug.
- Sponsor has not supported the research that preceded the study.

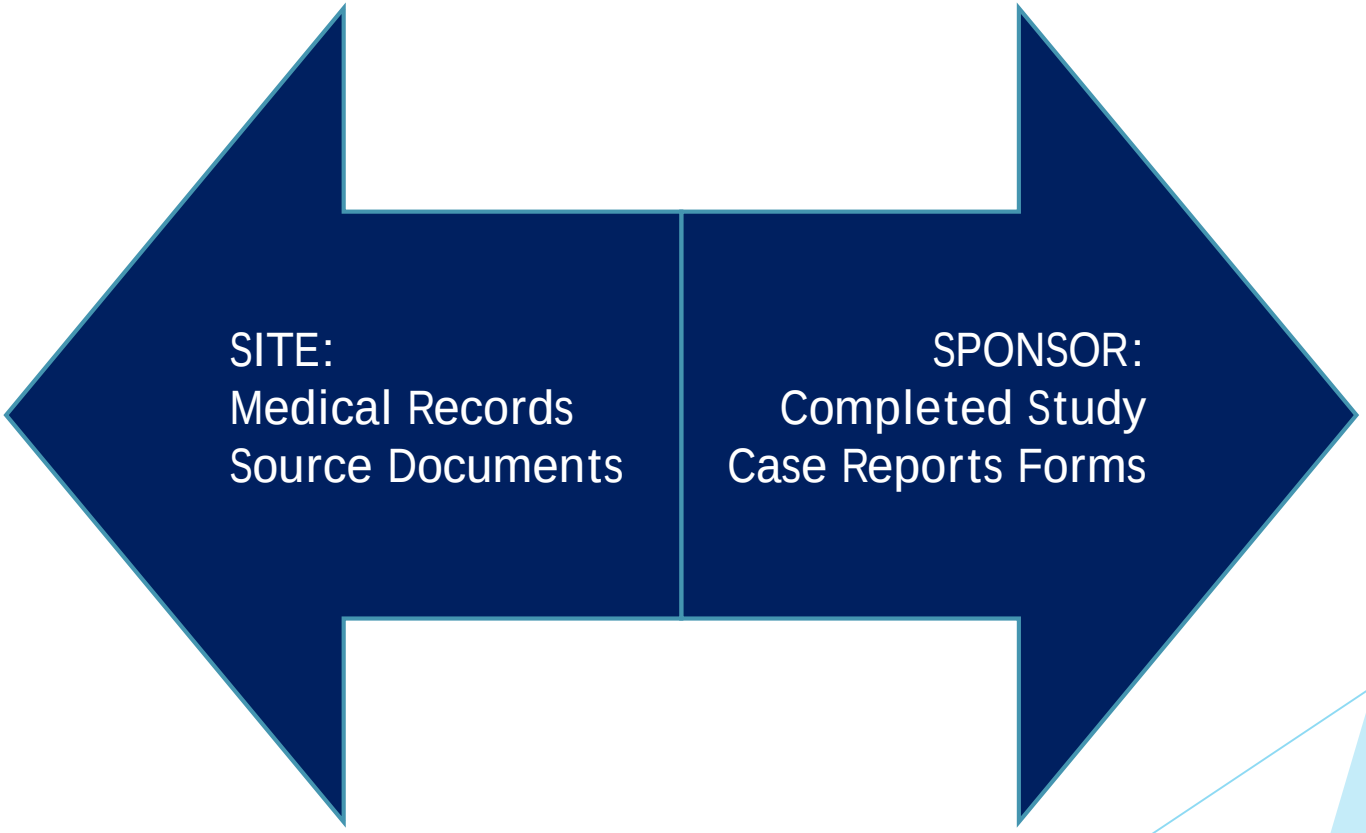
Rights in Data Generally

- Data itself is not protected by IP rights
- Can be information that is used to create IP
- Issue is usually control of information
  - Access can be restricted by contract (e.g., database subscriptions or confidentiality provisions in contracts).
  - Institutions need to retain uncontrolled use of its data to assure freedom to publish, to conduct future research, and to provide patient care.
  - Sponsors need to protect proprietary position
    - IP (maintain competitive edge = $ feasibility towards developing new drugs)
    - Protect integrity of trial outcomes (problems: early or inaccurate publishing)
    - Confidential Information of Sponsor (for competitive reasons)

Study Data and Results

- Study Data – all raw data, all information on CRF's (Case Report Forms)
- Source Documents – data recorded in patient medical records BEFORE it is entered into the CRF
- Study Results – aggregate of study data from all sites, OR a single site. Often addressed in the Publication Rights Section.

Who Owns - Site or Sponsor?



Key Contract Terms Governing Data

- Definitions
- Ownership or Access Rights
- Confidentiality
- Publication

Confidentiality and Publication Rights

- The key issues limiting publication rights of the Institution are:
  - Confidential Information and its definition
  - Permitted uses of Study Results and Study Data
  - Publication of a multi-center study by Sponsor
  - Tax exempt status requires “free and unfettered publication.”
  - Investigators must publish to be promoted (granted tenure)
    - If not promoted, they must leave the institution

Negotiation Tips and Potential Compromises:

- Scope of Data should be tied directly to data collected in the performance of the Protocol and delivered in accordance with the Protocol.
  - Include carve-out for publication in Confidentiality terms
  - Retention of right of Institution to use Data for non-commercial purposes.
  - Sponsor cannot require that publication be subject to granting of permission.
  - Sponsor cannot have editorial control over publication.