

# Clinical Trial Agreements: Best Practices for Effective Negotiations

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# Our Agenda

- Identify issues that typically slow down clinical trial agreements (CTA) negotiations
- Discuss key CTA provisions and how to reach consensus on the provisions
- Discuss best practices for ensuring efficient and effective negotiations

# Is there a more efficient way to negotiate CTAs?

- The number one enemy of sponsors is time
- Their goal is to get a clinical trial started as soon as possible, and ended as soon as possible.
- Institutions that want to be seen as desirable clinical sites want to be receptive to a speedy process

# Main Factors

- A clear process in which each side has those at the table who can agree on terms
- Fair clauses upon which the parties can agree
  - The same clauses slow down negotiations every time

# Process

- Figure out who the parties will be and how many agreements there will be
- Determine who needs to be at the table to make the decisions
- Be clear about the timeline for negotiations

# Identify the Parties

- Every study needs a sponsor and an investigator
- Institution is usually a hospital or medical center
  - Sometimes the Institution employs the investigator, other times the investigator has privileges at the Institution

# Identify the Parties

- Sometimes there is another party involved in the study
  - Investigator may belong to a group practice that is conducting the study and the investigator only has privileges at the Institution where the study take place
- Determine if another institution will become a third party to the CTA

# Identify the Agreements

- Sponsors need an agreement with the investigator to satisfy FDA rules
  - For drug trials this is satisfied by FDA form 1572, but there is no such form for device trials
- There needs to be an agreement between the Institution and Sponsor to cover payment, indemnification, IP rights, etc.



# Identify the Agreements

- Some clients prefer to have one agreement that includes the investigator obligations and the arrangement between the Sponsor and the Institution
- Some clients prefer to have a separate investigator agreement that is attached to the Institution agreement
  - Institutions often prefer this approach

# Identify the Agreements

- In any case, the investigator must sign as a party to an agreement that satisfies FDA regulations (21 CFR 812.43)
- Investigator must also agree to the terms of the Institution agreement, such as IP
  - Unless the investigator is an employee and the Institution's signature binds him/her

# Identify the Agreements

- Determine if a separate device purchase agreement (DPA) will be required
  - Often, a DPA will not be needed because the Sponsor retains ownership of the devices
- If the Institution requires a DPA, make this clear early on so it does not surprise the Sponsor later in the process

# Identify the Agreements

- In summary, get everybody bound to everything no matter how you divide up the contract
- Either have the investigator be a party to the CTA or have a separate investigator agreement signed by the investigator which includes all necessary FDA language

# Figure out the Process

- Often, the Institution's procedures will dictate the process for negotiating the CTA, budget, and DPA (if any)
  - Identify whether these negotiations can occur concurrently
  - Budget may be handled by a different department than the CTA
- Can the Institution negotiate the CTA and budget prior to IRB approval?

# Who needs to be at the table?

- If the Institution has the CTA first vetted by purchasing or clinical personnel who have no authority to make the decisions, it is doomed for delay
- Identify early on who can say the contract language is acceptable
- Put those people on each side in communication, if possible

# Contract Terms

- Identify the clauses typically slow down negotiations and find a fair ground
- If the Institution has required clauses, such as adherence to a religious code, present them early so the Sponsor can review and incorporate them as soon as possible

# Contract Terms

- Publication
- Use of and Access to Study Data
- Termination
- Intellectual Property
- Indemnification
- Subject Injury



# Publication

- Sponsor's interests:
  - Generate data to complete the study
  - Obtain regulatory approvals
  - Protect intellectual property
- Institution's interests:
  - Academic freedom and scholarly publication
  - Generate IP and new avenues for research

# Publication

- Sponsors usually place restrictions on the Institution's publication rights
  - Right of Sponsor to review and remove Sponsor confidential information
  - Delays to protect IP/file patents (e.g., 60 days)
  - No publication by Institution until publication of multi-site data

# Publication

- Institution typically requests the right to publish within a certain timeframe after study completion (e.g., 12 months), regardless of multi-site publication
- Parties should agree to reasonable timeframes for Sponsor's review and for Institution's publication

# Use of and Access to Study Data

- Sponsors need full access to data relating to the study
- Also need to ensure that FDA can access this information
- Institutions want to protect patient information and be able to use data for internal research and education

# Use of and Access to Study Data

- Sponsor should own case report forms
- Institution should own medical records
  - Definition of “Source Documents”
- Agreement should allow the Sponsor and FDA access to all study data, including medical records

# Termination

- Usually a boilerplate term, but it requires more consideration in the clinical trial context
- Termination is different from ending enrollment
- Institution must stop enrolling patients when the study reaches its limit

# Termination

- The CTA should not be for a fixed time, such as two years
- The obligations of the parties needs to continue until all follow up is complete
- The Sponsor must be able to terminate at any time, plus the Sponsor will want to terminate if the investigator is not available

# Termination

- I recommend termination when the study is closed and no further work is needed
- FDA will want continued follow up, so the study may go on for five more years
- This affects informed consent



# Intellectual Property

- In the old days, sponsors used to ask to own everything including the investigator's first born
- Institutions would come back with cries of “academic freedom” and demand all ownership
- Neither was helpful

# Intellectual Property

- Sponsors need to be free to market and cannot enter into agreements in which things invented on their dollar can block them from selling their products
- Institutions should not give up new cures to disease simply because they were discovered on a day they were working on a clinical trial

# Intellectual Property

- Institutions should retain rights to inventions that may come up that are not directly related to the device (e.g., a new surgical instrument idea that comes to a doctor while implanting)
- Academic institutions routinely ask for a license to inventions for use in research internal to the Institution

# Intellectual Property

- Usual middle ground:
  - Sponsors should own all improvements to their product
  - Institutions should own all else
  - All parties keep title to anything invented before the trial

# Sample IP Clause

“All ideas, inventions, improvements or suggestions, whether or not patentable, derived directly from work under this Agreement that relate to the Study (“Ideas”) shall belong to Sponsor. Other inventions made by the Investigator or Institution shall not be the property of Sponsor. Investigator and any persons who work under this Agreement agree to disclose and assign to Sponsor, any Ideas made alone or in conjunction with others under this Agreement. Ownership of inventions, technologies, processes, algorithms, ideas, techniques, discoveries, improvements, devices, products, biologics, concepts, designs, prototypes, samples, models, materials, drawings, specifications and other works of authorship existing as of the Effective Date, and all patents, copyrights, trade secret rights and other intellectual property rights therein (collectively, “Pre-existing Intellectual Property”), is not affected by this Agreement, and no party shall have any claims to or rights in any Pre-existing Intellectual Property of any other party, except as expressly provided in any other written agreement between two or more parties.”

# Indemnification

- Sponsors should be ready to stand behind their product and indemnify for any new risks it brings
- My opinion - indemnification should follow what each party controls

# Indemnification

- Sponsors should indemnify for later use of the data in getting FDA approval or marketing the product
- Sponsors should indemnify for problems with its device, injuries directly caused by its device, or injuries caused by a procedure required by the study protocol

# Indemnification

- Who should indemnify for risks of normal hospital care that are not part of the protocol?
- If a subject is in the hospital for study procedures, who takes normal hospital risks, such as infection?
- This needs to be negotiated



# Indemnification

- Sponsors should not have to indemnify for things the Sponsor does not control
  - Indemnification for “any claim resulting from the trial” would include a subject slipping on the ice in the parking lot
  - Hospital risks such infection cannot be mitigated by the Sponsor and should not be indemnified by the Sponsor

# Indemnification

- Many trials are not of a first generation device (e.g., pacemaker or heart valve)
- In these cases, the patient would be in the hospital anyway, getting some pacemaker or heart valve
- All the normal risks of doing so are not increased by the trial and should not be indemnified by the Sponsor

# Sample Indemnification Clause

“Sponsor agrees to indemnify, defend and hold harmless the Institution, its trustees, officers, agents and employees, and Investigator against any claims, suits or judgments made or instituted against Institution or Investigator to the extent they are caused by the defect or malfunction of Sponsor’s device under this Study, or by a procedure required by the Protocol, except to the extent that such claim or judgment is based upon negligence or misconduct by the Institution or Investigator or the failure of the Institution or Investigator to follow the Protocol.”

# Subject Injury

- For research involving more than minimal risk, FDA regulations require an explanation regarding availability of compensation and treatment for research-related injuries (21 CFR 50.25)
- FDA regulations do not require researchers, sponsors or institutions to offer payment for treatment of injuries

# Subject Injury

- CTAs vary significantly in terms of the Sponsor's coverage for subject injury costs
- Subject injury clauses raise more issues than we have time to discuss today

# Best Practice

- Be ready to make a deal
  - Do not assign the negotiations to someone who cannot agree to the terms
  - OR provide a direct link to someone who can
  - The worst delay is working up and down chains of command

# Use of Boilerplate

- We all use boilerplate clauses
- If you use them, say it upfront and do not add them to the agreement later in the process
- Again, if your institution requires a religious adherence clause, say it the first day and provide the text

# Use of Boilerplate

- Attorneys, do not saddle your negotiator with one-sided unworkable boilerplate terms that you know will never be accepted
- This just wastes everyone's time



# Best Practice

- Use faster methods of communication
  - Sometimes you can solve most of the issues by picking up the phone
  - Some issues fester because neither side can understand the motivation and purpose because they are not explained
  - Make a call, make a friend

# Best Practice

- Consider making a first call where you discuss your key issues before they appear in redlines
- An early warning as to the important issues can speed the process and avoid delays later on

# Best Practice

- It is difficult to compromise and give somebody what they want if you don't know what it is that they want
  - You may not agree, but you can never make an offer attractive to the other side if you do not know what they want
- If you conceal your want, it is hard to get it

# Best Practice

- Be clear and transparent about the process within your company or institution
- Identify the key people who will be responsible for the negotiations
- Be upfront about any expected delays

# Best Practice

- **Be reasonable.** Start with a position near where you know you will end up
- Trying to take an outrageous stance rarely draws the other party to you
- It just causes delay

# Questions?



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