Clinical Trial Agreements

A Moderated Discussion

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Disclaimer

The opinions expressed in this deck are those of the presenters and do not reflect the opinions of their employers. Nothing in this deck should be construed as legal advice.
The Preamble

Who are the parties?
1. Sponsor
2. Institution
3. Principal Investigator (PI)
4. Contract Research Organization (CRO)
5. Site Management Organization (SMO)

Common Issues:
1. If there is a CRO or SMO what is its role?
2. Can the PI be named as a separate party? Is he or she an employee of Institution?

The WHEREAS Clauses

The WHEREAS clauses can help address some common issues:
- What is the PI’s relationship to Institution?
- What are the roles of the SMO and CRO?

The WHEREAS clauses can also:
- Frame the agreement; and
- Add necessary definitions.
Services and Personnel

• Services
  – The performance of the Protocol, as amended.

• Personnel
  – Who is responsible for the performance of the Services?
  – Can include PI, Sub-Investigators, Institution employees and contractors, those working under the PI’s direct supervision.
  – Can cascade throughout (e.g. indemnification, debarment).
  – This is the first opportunity to limit Institution’s liability for third parties like CRO or SMO.

Payment/Compensation and Expenses

• Payment for Services
  - What is the trigger for payment?
    - Receipt of case report reforms (CRFs) by Sponsor?
    - Approval of data by Sponsor?
    - Electronic Data Capture (EDC) entry?
    - Penalties for late payment?

• Reimbursement for expenses
  – Are all expenses stated in the budget?
  – Is there a catch-all for expenses not included in the budget but approved by Sponsor?
Medicare Coverage Analysis (MCA) and Fair Market Value (FMV)

• Have you performed an MCA?
  – Are there promises to pay contained in the CTA that would prevent billing government payers?
  – Are the promises to pay in the ICF?
  – Conditional payment language?

• Fair Market Value Statement?
  – Anti-Kickback Statute (AKS) and Stark implications.

AKS and Stark

AKS

Prohibits offering, paying, soliciting or receiving anything of value to induce or reward referrals or generate Federal health care program business

Stark

Prohibits physicians from referring their patients to other entities for designated health services (“DHS”) (e.g. labs, radiology services) payable by Medicare when the physician or an immediate family member of the physician has a direct or indirect financial relationship with the entity.

Safe Harbors apply

- Services must be stated in writing and appropriate to accomplish the business task
- Payment must be FMV
- Term of at least 1 year

Term:

This Agreement shall be effective as of the Effective Date until the later of one (1) year or until the Services are completed.
Medicare Secondary Payer (MSP) Rule

The MSP provisions protect the Medicare Trust Fund by ensuring Medicare does not pay for items and services when other health insurance coverage is available.

When the CTA or ICF contains a promise to pay for an item by Sponsor, Medicare cannot be billed for that item.

Commonly used problematic language:

Clinical Trial Agreement:

- Payment is intended to cover all costs for the performance of the Study.

Informed Consent Form (ICF):

- Subject shall not be liable for any costs as a result of participating in the Study.
- All services provided as part of the study shall be at no cost to you.

The Sunshine Act

Section 6002 of the Affordable Care Act and all applicable proposed and final rules and regulations promulgated thereunder (the “Sunshine Act”) requires that applicable manufacturers (Sponsors) report:

- the research-related transfers of value
- to “covered recipients” (e.g. “teaching hospitals” and PIs)
- made pursuant to a written agreement between Sponsor and covered recipients

Note: payments made by a CRO or SMO on behalf of Sponsor do not relieve Sponsor of the duty to report.
Sunshine Act Reporting

Sponsors must include:

- PI Name
- Aggregate amount of research payment
- Name of the study
- Name of the related covered drug, device, biological or medical supply

Note: this obligation belongs to the Sponsor and not the Institution or PI.

Confidentiality

- Definition of Confidentiality?
  - Protocol, Study data, Inventions
- Who is the “Receiving Party?”
- 1-Way or 2-Way?
  - Will site provide confidential information to Sponsor?
- Obligation to mark?
- Length of confidentiality obligation?
- Permitted Use?
- Rights to disclose?
- Exceptions?
- State Open Records Laws considerations?
- Who owns which classes of information?
  - Medical Records/source docs should always be property of PI/Institution.
Publication

- Multi-center publication?
- What if no multi-center publication?
- Review period?
- Sponsor’s right to comment?
- Sponsor’s right to delay for patent purposes?
- Should there be a reduced review period for abstracts/posters?
- Does your Institution have publication policies?
- Does your Institution’s mission require certain publication rights?

Inventions/Intellectual Property (IP)

- Use of the Study Drug
  - Only for the performance of the Protocol?
- Sponsor/Institution/PI rights?
  - Existing IP?
- Directly related to the Study Drug, Protocol or other Sponsor Confidential Information?
- Independently developed IP?
- Institution/PI obligation to notify?
- Sponsor right of first refusal?
- Institution/PI non-exclusive license to use for academic or patient care purposes?
- Sponsor non-exclusive license to use for non-commercial, internal research and development purposes?
- Does your Institution have IP policies or requirements?
Inventions/IP – Additional Considerations

- Tax Implications for some Institutions that receive government funding (including government bonds)
  - Does your Institution require PIs to own IP and Study data?
    - Is there an exception for CTAs?
  - What rights does the Sponsor receive?
    - Non-exclusive license?
    - Right to negotiate an exclusive commercial license?

  - If research is funded using federal funds Sponsor or Institution can own the “subject inventions” but the government receives “march in” rights
  - Organizations must:
    - Include the patent rights clause in any subcontracts;
    - Report subject inventions to the sponsoring agency;
    - Elect in writing whether or not to retain title;
    - Conduct a program of education for employees regarding the importance of timely disclosure; and
    - Require certain employees to make a written agreement to protect the government’s interest in subject inventions.

Monitoring Visits and Regulatory Audits

- Advantages of separating the 2 concepts?
- Access to Institution
  - Who?
  - When?
- Rights to access EMR?
- Compliance with Institution policies?
- PHI considerations?
- Does the Sponsor deserve the same access as regulatory agencies?
- Right to copy records?
- Right to take records off site?
Record Retention

• Institution/PI’s obligation to maintain study records?
• Scope and duration?
• Obligation to provide notice prior to destruction?
• Can your Institution comply with Sponsor demands?

Publicity

• Any party’s right to use the other parties’ (including PI) names
• clinicaltrials.gov considerations
• Institution internal or public disclosures required
Term and Termination

• Length of term?
  • Until Services/Study are/is complete?
  • 1 Year from the Effective Date?
  • Stark implications?
• Is this a master? If so, how are work orders affected?
• Rights to terminate?
• What if the PI leaves the Institution?

Indemnification by Sponsor

• Should Sponsor indemnify for injuries, causes of action and costs for “claims” caused by the following?
  – Study Drug/Device
  – Performance of the Protocol
    • Or non-standard of care procedures required by the protocol
  – Sponsor and its representatives’: negligence, willful malfeasance, breach of the agreement or lack of adherence to applicable laws
  – Sponsor and its bona fide collaborators’ use of Study data or Inventions
Indemnification by PI and/or Institution

• Is the PI a separate party? Can he or she indemnify?
• Insurance concerns?
• Will Institution allow indemnification of Sponsors?
• State law concerns?

Indemnification by PI and/or Institution (cont.)

• Should PI/Institution indemnify for injuries, causes of action and costs for “claims” caused by the following?
  – PI/Institution and its representatives’ negligence, willful malfeasance, breach of the agreement or lack of adherence to applicable laws
Indemnification Considerations

- Definitions
  - Sponsor Indemnitees
    - those acting on Sponsor’s behalf in the performance of the Study
    - e.g. Sponsor and its Affiliates, CRO, etc. and their respective employees, contractors, representatives and agents
  - Institution Indemnitees
    - those acting on Institution’s behalf in the performance of the Study
    - e.g. Institution, PI, Sub-Investigators, Institution’s IRB, Institution Affiliates and their respective employees, contractors, representatives and agents

- Exceptions – neither party shall be obligated to indemnify to the extent that a Claim was caused by the other party’s (or any indemnified party’s) negligence, willful malfeasance, lack of adherence to applicable laws or breach of the Agreement.

Subject Injury Clause

- What costs should the Sponsor be responsible for?
- Should reimbursement be limited to Institution?
- Actual costs or a predetermined reimbursement methodology?
- What about if the Study subject does not follow instructions?
- Can the Institution be required to bill third parties before the Sponsor becomes responsible?
  - How does the MSP rule apply?
  - How about just non-government payers?
- Do the standard exceptions apply?
- MMSEA concerns?
Subject Injury Clause Example

“Sponsor shall reimburse Institution for the actual cost of services provided to a Subject if the Subject is injured as a result of taking the Study Drug according to the Protocol but only if the Subject’s insurer denies the claim for the service(s).”

Medicare, Medicaid and SCHIP Extension Act (MMSEA)

- Section 111 requires Sponsors to report to CMS payments for treatment of subject injuries where the subject is a Medicare beneficiary
  - Information to be reported includes PHI and SSNs

- Sponsor’s template CTA (and ICF) requires sites (or Subject) to provide information required for Sponsor to meet its reporting obligations

- After execution of CTA, Sponsor may require sites to provide SSN and other information on every subject enrolled
  - Does this request present any regulatory issues?
Insurance

• Who are the parties and do they each have their own insurance obligations?
• Survival beyond termination or expiration of the CTA?
• Does any party’s insurance limits serve as a limitation on their liability?

Limitation of Liability

• Exclusion of special damages?
  – Exception for indemnification/3rd party claims?
  – Exception for confidentiality breach?
  – Exception for fraud, intentional misconduct, etc.?

• Cap on total damages?

• Does your insurance carrier require a specific limitation of liability?

• Does your Institution require a specific limitation of liability?
Debarment, Ineligible, Convicted

- Who are the parties and are they each responsible for their own representations, warranties and reporting obligations?

- What about actions or investigations that could result in debarment, ineligibility or a conviction?

- How long will the obligation to report survive expiration or termination of the CTA?

- Does your Institution’s exclusion check process allow you to comply with the CTA terms?

IRB, Informed Consents and HIPAA Authorizations

- Whose obligations it is to have the Protocol approved by the IRB? Does this apply for the ICF and HIPAA Authorization?

- Who shall be responsible for obtaining an ICF and/or HIPAA Authorization from each Study subject?

- What role will the Sponsor play in submission to IRB and the final approval of templates?

- Does you Institution/IRB allow for ICF and HIPAA Authorization to be combined?
Financial Disclosures

- Whose responsibility is it to collect and provide financial disclosures to the Sponsor?

- How long does the obligation to report changes survive expiration or termination of the CTA?

Budget Exhibits

- Budget Exhibits can include language invoking MSP issues

- OIG has been hostile towards “milestone” based budgets as they are not as transparent as “line item” budgets
  - Not per se a problem but “line item” budgets allow for easier justification of FMV and dissuade double billing

- CMS has made statements that conditional payment language means Institutions cannot bill
  - e.g. “Sponsor will pay for items not covered by subject’s insurance”
  - CMS retracted those statements but they could be re-issued (consistent with MSP rationale)
  - Look back period could extend to 7 years
**Miscellaneous Provisions**

- **Survival**
  - Do the sections your Institution needs to survive actually survive?
  - indemnification, subject injury, insurance
- **Assignment**
  - Can the Institution assign to an affiliate?
  - Can the PI or Institution assign another PI?
- **Separate legal representation**
  - Can be important if PI is not an employee of Institution
- **Applicable law, venue**
- **Waiver of a jury trial**

**Device Trial Considerations**

- **No 1572**
- Investigator statements required
- Budget considerations
- Medicare Coverage Analysis – As of January 1, 2015, approval for billing Medicare is obtained by Sponsor from the CMS Central Office.
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