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How to Draft Clinical Trial Agreements

(A Guide for Sponsors)

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INTRODUCTION

Clinical Trial Agreements ("CTAs") can be surprisingly complex documents with numerous legal issues, particularly in the setting of a multi-center trial for a new drug product candidate. This outline highlights the principal issues typically arising in a CTA and some of the considerations for companies sponsoring pharmaceutical trials ("Sponsors") in addressing these issues.

GENERAL POINTS

- **Parties**. Who are the parties to the CTA? Will it be the Sponsor or a clinical research organization engaged by that Sponsor? On the other side, will it be a medical center (the "Center") or an investigator at that Center (the "Investigator") or both? Some Centers insist that the CTA be only with the Investigator, which raises a number of issues (see Indemnification and Insurance below).
- **Scope of Work**. A careful definition of the work to be performed by the Center and Investigator is important. Typically, a clinical study protocol for the clinical trial approved by that Center's institutional review board ("IRB") will be the basis for defining the scope of work. If an Investigator's brochure has been prepared by the Sponsor, this should be referenced in the CTA.
- **Principal Investigator**. The identity of the Investigator is generally of keen interest to the Sponsor. The CTA should address what happens if that Investigator is unable to complete the trial.
- **Term of Agreement**. The term of the CTA should be defined. Typically, this will be tied to completion of the trial.
- **Budget and Payments**. The CTA should include a budget for all expenses of the trial at the Center (typically inclusive of the Center's overhead charges). A schedule of payments against this budget should be included, with at least some amounts held back by the Sponsor for payment upon receipt of all completed patient case report forms and delivery to the Sponsor of all other contemplated data and reports and return of, or accounting for, unused product inventory and other Sponsor provided equipment and materials that are not to be retained by the Center or Investigator.
- **Confidentiality**. The Sponsor will be seeking customary confidential treatment language in the CTA for all or many aspects of the trial. However, this will need to be balanced against the Center's need to protect the health and safety of its patients in the trial with respect to matters such as unexpected side effects encountered in the trial (see also Publication below).
- **Regulatory Compliance by Center and Investigator**. The Sponsor will want the CTA to address the obligations of the Center to satisfy certain internal and other federal, state and local regulatory requirements. These will, at a minimum, include compliance with IRB approval requirements, obtaining appropriate informed consent forms from patients in the study, FDA good clinical practices, and HIPAA compliance. The CTA should include representations by the Center of its compliance with the debarment provisions of the Generic Drug Enforcement Act.
- **Trial Product and Supplies**. The CTA should clarify the Sponsor's responsibilities for providing supplies of the product candidate being tested and any related equipment or materials for the trial and whether this is at the Sponsor's expense. The disposition of any unused product supply, equipment or materials at the end of the trial (i.e., return to the Sponsor, verified destruction or retention by the Center) also should be addressed.
- **Competing Trials**. If the Sponsor is concerned that the Center or Investigator may conduct other trials concurrently with the Sponsor's trial that could compete for patients to be enrolled or raise other issues from the Sponsor's viewpoint, the CTA should include appropriate limitations on these activities to the extent that the Center and Investigator are willing.

- **Recordkeeping and Reporting by Center**. The Sponsor will need to have the Center and Investigator maintain and update various records in connection with the trial, including case report forms and patient medical records. The specific records and the time period for keeping these records should be specified based on the type of trial and applicable FDA and other regulatory requirements. Should patients suffer serious side effects in the trial, the Center and Investigator should be required to immediately inform the Sponsor. The CTA should define what constitutes a serious side effect in light of the importance of these notification requirements.
- **Sponsor Monitoring and Auditing**. The Sponsor's right to access all information resulting from the trial (subject to the trial patients' confidentiality) should be set forth in the CTA. The CTA should also give the Sponsor the right to audit the Center's and Investigator's compliance with the trial protocol and recordkeeping procedures and accuracy. The Center should be required to notify the Sponsor of any FDA or other regulatory agency audit of the trial, the Investigator or the facilities at which the trial is being conducted.
- **Termination of Agreement**. The CTA should provide for what events, other than completion of the trial, will trigger a termination of the CTA. Termination for cause, such as material breach of the terms by a party or IRB or other regulatory withdrawal of approval of the trial, should be defined. The Sponsor will also want to be able to terminate without cause since it may abandon the trial for various reasons. The Center may also seek this right, which can be a significant issue for the Sponsor. The allocation of compensation to the Center in the case of an early termination should be covered in the CTA.
- **Publication of Trial Data**. The procedures for publicizing the results of and data from the trial should be governed by the CTA. In a multi-center trial, a lead or primary paper typically will announce and describe the trial results. The Sponsor will want to control the designation of the author of this publication and limit other publications coming out before the lead publication. The Sponsor should retain a right to review all publications to protect confidential information and any patent positions it has arising from the trial (see "Intellectual Property" below). The trial data and results that can be published will need to be excluded, but carefully, from protected confidential information.
- **Intellectual Property**. The CTA should specify who owns the intellectual property arising from the trial and provide for the cooperation of the other party in perfecting these rights. Will the Sponsor retain all of these rights or a more limited set of these rights? If the Center's personnel are responsible for the invention, will the Sponsor only have some form of an option (to be defined in the CTA) to acquire a license to this invention?
- **Indemnification**. The Sponsor and the Center will both be seeking indemnification for liabilities arising out of the trial. If the Center is a state institution, there may be severe limitations on its ability to provide an indemnification. If only the Investigator is a party to the CTA, this will also pose indemnification issues for the Sponsor. The indemnification provided by the Sponsor for patient injuries needs to be carefully limited to injuries directly caused by the product being tested versus such issues as underlying illnesses, standard of care treatments during the trial or deviations from the established protocol. What offsets to the patient's damages will reduce the amount of the indemnification required of the Sponsor (insurance recoveries, etc.)?
- **Insurance**. The Sponsor will be required to maintain liability insurance unless it is able to persuade the Center that it is sufficiently strong financially to self-insure. The Sponsor will need to coordinate the amounts of insurance and time periods for which the CTA requires this insurance to be in place with its insurance professionals. Typically (but not always), the Center will self-insure. If the Center is not a party to the CTA, the Sponsor will want the CTA to require the Investigator to obtain liability insurance in sufficient amounts.
- **Miscellaneous Clauses**. The CTA should address, at a minimum, the following miscellaneous provisions:
    - *Assignment*. The Sponsor will want the CTA to be assignable by it but not the Center.
    - *Independent Contractor*. The CTA should confirm the independent contractor nature of the relationship between the Sponsor and the Center and Investigator.
    - *Governing Law and Dispute Resolution*. The Center will generally ask for the governing law to be its home state's law. This usually should not be a material issue for the Sponsor, who will be more concerned with a convenient venue for dispute resolution, particularly in the case of a multi-center trial. The CTA also should address whether mediation or arbitration will be used, which may be beneficial for the Sponsor.

CONCLUSION

The preparation of a CTA from a Sponsor's viewpoint will be a coordinated effort by the Sponsor's medical, regulatory, manufacturing, accounting and insurance advisors with its clinical research organization for that study. As the CTA is prepared, the legal issues outlined above, among others, will need to be considered and addressed as appropriate.

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