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Model Clinical Trial Agreement Clauses for Oncology

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In 2001, then-U.S. President George W. Bush asked Robert A. Ingram, then-CEO of Glaxo Wellcome, to convene and chair the CEO Roundtable on Cancer ("CEO Roundtable"), a nonprofit organization dedicated to taking "bold and venturesome" steps to protect the members' employees from cancer and furthering the fight against cancer.

The CEO Roundtable's Life Sciences Consortium (LSC) includes representatives from the major stakeholders (sponsors, research institutions, research sites, and one contract research organization (CRO)), as well as the National Cancer Institute (NCI). As one of its bold and venturesome steps, the LSC, in collaboration with the NCI, drafted a document, "Proposed Standardized/Harmonized Clauses for Clinical Trial Agreements" (the Proposal), for the purpose of streamlining negotiation of cancer clinical trial agreements (CTAs).

All parties in clinical research would rather conduct the research than argue over contractual language. The challenge, of course, is to develop standard language agreeable to all parties. The Proposal has largely accomplished this objective for the core sections of CTAs.

The LSC created the Proposal to address the needs of cancer research. It is also applicable to research in other therapeutic areas. The Proposal shows an admirable degree of brevity and simplicity. However, as in any standardization project, it no doubt includes many compromises that may not reflect the perspective of any LSC member.

The Proposal provides clauses for intellectual property, confidentiality, data, publication rights, indemnification and subject injury. This article discusses Part I of the Proposal: language for company-sponsored research. Part II of the Proposal includes language for investigator-initiated research.

With no disrespect to LSC's impressive accomplishment, this article identifies potential improvements from the perspective of institutions with charitable and academic missions. The discussion below excerpts and summarizes the Proposal's language. The full text of the Proposal can be found at http://cancercenters.cancer.gov/documents/StClauses.pdf. This article uses the Proposal's naming conventions of "Research Institution" for site and "Company" for sponsor of a clinical study.

Inventions

The proposed language defines the term "Inventions" as "all inventions, discoveries and developments conceived, first reduced to practice, or otherwise discovered or developed by either party or any of such party's personnel in the performance of the Study." Inventions are owned by the party that made the invention; jointly created inventions are jointly owned. The Research Institution must disclose inventions and assign all rights, title and interest in such Inventions to the Company. In return, the Company grants to the Research Institution a perpetual license to use Inventions for "internal, non-commercial research and for educational purposes."

The definition of "Inventions" is extremely broad. By including mere concepts and ideas and framing the discovery as occurring "in performance of the Study," the language covers discoveries that are wholly unrelated to the Company's pre-existing intellectual property. When the discovery is anticipated by the Protocol, or when it directly relates to the study article as it was conceived by the Company, this assignment of rights is generally accepted.

Similarly, if Company personnel materially contribute to the Invention, joint ownership with assignment is reasonable. But, if in the course of the study, the Principal Investigator has an "ah-ha" moment and discovers a previously unknown (and unexpected) connection, the Principal Investigator should enjoy the fruits of his or her inventive capabilities.

Companies typically argue that such inventions would not occur in the absence of the clinical trial, which the Company is paying the Research Institution to conduct. This argument would be more plausible it were supported by the study budget. However, few, if any, study budgets include a line item for "invention services." Absent compensation, the Sponsor should not gain the economic and competitive benefit of the Principal Investigator's inventive capability.

In some cases, the license granted to the Research Institution should include treatment purposes. For example, if the Principal Investigator develops a method that results in better patient outcomes, ethical considerations support ensuring that the method can be used for the benefit of the Research Institution's patients. This right to use the invention for treatment purposes is most clear in the case of "method of use" inventions.

Data

The definition of "Study Data" to include "all records and reports, other than Medical Records, collected or created pursuant to or prepared in connection with the Study…" captures purely administrative internal documentation of the Research Institution and Principal Investigator. Modifying this language to include only records and reports that are required by the Protocol or other written direction from the Company avoids this overly expansive interpretation.

Confidentiality

The confidentiality provisions contemplate that only the Company has Confidential Information to which the Research Institution and Principal Investigator will be exposed. However, in reality, the exposure occurs in both directions, so the confidentiality provisions should be reciprocal.

The proposed language permits the Research Institution and Principal Investigator to use the Company's Confidential Information only for performance of the Study, and to disclose Confidential Information only upon the Company's written consent, or as required by law or regulatory authority. There are other situations, however, in which it may be necessary for the Research Institution or Principal Investigator to use or disclose the Company's Confidential Information. For example, if a study participant becomes ill in another town, disclosure of information related to the Study may be necessary to permit diagnosis or treatment of the patient. Similarly, if research personnel are injured by the study article, disclosure of details related to that article may be necessary. The language should be modified to permit these types of use and disclosure.

The proposed language also mandates notification to the Company if a third-party seeks to compel disclosure of Confidential Information, and that compelled disclosure must be limited to "only that portion of the Confidential Information which is legally required to be disclosed." There may be times when the Research Institution or Principal Investigator is unable to comply with this obligation, for example, when served with a search warrant by a law enforcement agency. Similarly, reasonable minds can differ on the scope of mandated disclosure, particularly when presented with legal process. The language should therefore be modified to accommodate the reasonable judgment of the party served with the legal process. Finally, the provision requires the Research Institution and Principal Investigator to return or destroy all Confidential Information other than Study Data upon termination of the

Agreement or written request by the Company. However, retention of such information may be required by law or regulation, or otherwise necessary for compliance or legal purposes. The standard language should be modified to reflect this necessity.

Publication Rights

The right to publish the results of research — whether the findings are positive or negative — is essential to academic and charitable institutions that engage in research. Publication is also important for public health. Positive findings are of obvious interest and negative findings direct research away from dead ends. The Proposal recognizes the importance of publication, and for the most part, does a good job of balancing the interests of the Company and the researchers.

As is common in CTAs, the proposed language gives the Company the right to require redaction (removal) of Confidential Information, other than study data, from proposed publications. There are times, however, when redaction could lead to inaccuracy or a lack of clarity. This concern can be addressed by including language to the effect that redaction is not required if it would lead to scientific or legal inaccuracy, or would cause the publication to be incomplete or misleading.

In multicenter studies, the Company typically wants results first to be published in a multicenter publication. This is understandable, as the results of individual sites may not fully reflect the findings of the overall study. As is common in CTAs, the proposed language requires that researchers not publish independently until sufficient time has passed to permit preparation of a multicenter publication or abandonment thereof. However, it has been suggested that a Company may sometimes drag its feet to delay publication of unfavorable results. To address this concern, the Company should agree to diligently pursue completion of the study, database lock, and submission of the multicenter article.

There may be times when single-site results are so significant that public health interests mandate disclosure without delay. The Company should permit early disclosure of such results, after notice to and consultation with the Company.

Limitations on researcher interactions with the media during a study are often desired by the Company to avoid early and incomplete release of study information and to protect against securities law violations. The proposed language thus prohibits "…interviews or other contacts with the media… related to the Study, the Study drug/Study device, Inventions, or Study Data without the prior written consent of Company." This provision inadvertently prohibits interviews intended to notify the community of the availability of the study for subject recruitment purposes. Clarification of the intent of this section would be helpful.

Finally, the proposed language states that the Company will register the Study and "report the results of the Study publicly when and to the extent required by applicable law and regulations." Registration and release of study results are necessary for important reasons other than compliance with law: Academic and charitable research institutions must publish to fulfill their missions. Principal Investigators publish to expand scientific knowledge and advance their careers. Failure to publish negative study results wastes the sacrifice made by study subjects who endured unsuccessful treatment, and may cause future useless sacrifices. Most reputable peer-reviewed journals require study registration for publication. Measures to protect academic freedom may also be a condition of funding for the Research Institution by philanthropic organizations. This provision should be modified to state that the Company will register the study as required by law or as necessary to support institutional funding requirements or facilitate publication of Study results, and should make a firm

commitment to publish (or at least make a diligent attempt to publish) the results of the study, whether favorable or not.

Subject Injury

The Proposal states that the Company will reimburse the Research Institution "for the direct, reasonable and necessary medical expenses incurred by Research Institution…" This provision should state explicitly that it covers the Research Institution's payments to other parties and its own standard charges. In addition, the provision should be expanded to include charges by third-party providers directly to the injured subject.

The Proposal states that compensation for care will not be provided "…to the extent that such adverse event, illness or personal injury is caused by… failure by Research Institution, Principal Investigator, or any of their respective personnel to comply with this Agreement, the Protocol, any written instructions of Sponsor regarding the Study, or any applicable law, regulation or guidance… or negligence or willful misconduct…" This provision should make an exception for deviations deemed by the Principal Investigator or research staff to be necessary to avert imminent harm to the subject. Further, failure to comply with written instructions should limit compensation only if those instructions are consistent with the Protocol and Agreement.

Indemnification

The indemnification provision describes circumstances in which the indemnity is limited or void. As is customary, cooperation with the Company's defense is required. The provision requires "full" cooperation, which should be modified to exclude disclosure of information that is privileged under law, such as attorney-client communications and peer review proceedings. Failure to notify the Sponsor of the claim in a timely manner should limit indemnity only to the extent that such failure materially and irreparably prejudices the defense. Similarly, failure to "fully" cooperate should likewise only limit, not eradicate, the obligation to indemnify.

The provision gives the Research Institution and Principal Investigator the customary right to retain counsel on their own behalf. If this occurs, the parties should cooperate in the defense to the extent their interests are aligned and so long as such cooperation would not break the attorney-client privilege.

Conclusion

Standard CTA language that is readily accepted by sponsors, research institutions, and principal investigators will help minimize the time and cost necessary to reach agreement. The LSC Proposal is a valuable step toward this goal. This article suggests improvements that would benefit academic and charitable research institutions. Innumerable other modifications could be, and perhaps have been, considered by the LSC working group. In any case, each institution, sponsor and principal investigator must evaluate the provisions to ensure they are acceptable within the context of completing clinical research studies in a timely and ethical manner.

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