

The Evolution of the Council of Academic Hospitals of Ontario Statement of Principles – A Successful Harmonization Initiative

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Authors' Note

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Abstract

To improve efficiency, consistency and transparency in clinical trial contract negotiations with industry sponsors, a Council of Academic Hospitals of Ontario (CAHO) committee facilitated the development of standard principles for member hospitals to follow during contract negotiation. Hospitals were encouraged to provide a link to the CAHO document on their websites, which facilitated greater transparency. The public availability has allowed institutions in other jurisdictions, as well as community hospitals in the province, to align their standards with those of Ontario academic hospitals.

Keywords: research administration, clinical trial agreement, harmonization initiative

Introduction

To improve efficiency, consistency and transparency in clinical trial contract negotiations with industry sponsors, a Council of Academic Hospitals of Ontario (CAHO) committee facilitated the development of standard principles for member hospitals to follow during contract negotiation. The principles are available on-line for reference by institutions and industry (Slutsky et al., 2010). Hospitals were encouraged to provide a link to the CAHO document on their websites, which facilitated greater transparency. This living document was most recently updated in May 2010, and comments are welcome at any time. The public availability has allowed institutions in other jurisdictions, as well as community hospitals in the province, to align their standards with those of Ontario academic hospitals.

A strong competitor in the clinical research field, Ontario brings a wealth of resources to the table, including 25 CAHO member hospitals, each with a strong focus on research and innovation; a large and diverse patient population to draw from, and a mandate from the Ontario Government's Ministry of Research and Innovation to establish Ontario as a globally recognized knowledge based economy (Queens Printer for Ontario, 2010).

To continue to build the foundation of research and innovation needed to draw industry-sponsored research to the province, the CAHO aimed to streamline the contract negotiation process to effectively address one of the most important factors driving clinical trial competitiveness today – speed (Ferris, et al., 2009). Outlining hospital contract standards allows companies to develop or modify their contracts to reduce or eliminate negotiation time, with the goal of starting trials more quickly.

Industry sponsors were consulted as the standard principles evolved. A draft document sent to four pharmaceutical companies received positive feedback. Input regarding indemnification, intellectual property and privacy provisions was considered and incorporated into the principles document. (Moldofsky, Arts, & Slutsky, 2010).

The CAHO statement is accessible to everyone via the internet and invites feedback via an email address. Sponsors are now working collaboratively to agree upon and document industry principles. When this document is complete and publicly available, sites will have greater clarity and consistency on sponsor objectives, and another tool to facilitate communications between parties.

CAHO Principles in the Context of Other Harmonization Efforts

Other harmonization initiatives such as the Model Agreement Group Initiative in the United States (MAGI, 2011), the United Kingdom's Clinical Research Collaboration's (UKCRC) Industry Collaborative Agreements Report for the Development of Model Agreements for Collaborative Commercial Research, and Medicines Australia's Clinical Trials Research Agreements (Medicines Australia, 2011) also present principles, standard agreements and contract language. Unlike those efforts, CAHO does not provide sample

language but instead outlines important terms a clinical trial agreement should contain. The intent of this document is two-fold:

1. To provide guidance to Ontario academic hospitals when reviewing industry-initiated clinical trial agreements.
2. To provide guidance to industry sponsors who wish to engage Ontario academic hospitals in clinical trials so they may better understand the common principles that underlie such clinical trial contracts.

A brief discussion of four significant principles, publication rights, intellectual property ownership, confidentiality and indemnification, will help illustrate this.

For academic hospitals with a strong research mandate, publication rights are paramount. Like the MAGI, UKCRC and Medicines Australia initiatives, CAHO believes that sites need to retain their ability to publish study results, positive or negative, within a reasonable time frame; however, the acceptable timeline varies slightly among groups. Medicines Australia's Standard Clinical Trials Research Agreement for Commercially Sponsored Trials allows for publishing two years after study completion or the publication of the results of the multi-centre study. (Medicines Australia, 2011). The UKCRC timeline is not specified in days, but stipulates that publication will be upon completion "of the Clinical Trial, and any prior publication of multi-centre data, or when the Clinical Trial data are adequate (in Sponsor's reasonable judgment)." (United Kingdom Clinical Research Collaboration, 2005). MAGI outlines timelines for review but does not identify any parameters for the timing of the initial publication from study completion. CAHO sites will only accept an 18-month delay from study completion. CAHO sites are happy to allow industry partners to copy and distribute these publications, provided proper acknowledgment of authorship is provided.

Intellectual Property ownership and rights are another important component in a clinical trial agreement. The CAHO document aligns with the MAGI, UKCRC and Medicines Australia beliefs that this part of the agreement is context-specific, depending on which parties developed the protocol, with a range of options including site ownership, joint ownership, or industry ownership, with the site retaining the option to use the intellectual property for internal research, academic and patient-care purposes.

Both sites and industry have a vested interest in protecting their confidential information. CAHO encourages member hospitals and industry partners to agree on a reasonable term of confidentiality (10 years maximum) and to maintain the confidential information they receive using the same degree of care as they use with their own information. Medicines Australia does not limit the term of confidentiality. The UKCRC (2005) Model Clinical Trial Agreement for England has a 10-year confidentiality term; MAGI (2011) suggests 3 to 10 years is common, but its template leaves a blank so the sponsor and site can come to their own agreement.

Permitted disclosures of confidential information must include the ability to disclose information to potential study subjects during the recruitment process, or to study subjects who are or were enrolled in the study, particularly if the information relates to their health, safety, or diagnosis. THE UKCRC and Medicines Australia have similar terms to CAHO and MAGI. The MAGI (2011) document has similar parameters but addresses some additional reasons for disclosure the CAHO principles do not: disclosure to third-party payors if required to determine coverage, to protect public health or the health of third parties exposed to the study product, for peer-review and to other scholars wishing to verify study results.

The CAHO principles require a sponsor to provide indemnification for any claims caused by or arising out the conduct of the study according to the protocol, the sponsor's negligence or intentional wrongdoing, and the sponsor's use of the study results. The UKCRC's Industry Collaborative Agreements Report acknowledges that indemnification is a "contentious area and one that will need to be carefully handled in a new model agreement" (UKCRC, 2005). MAGI addresses the same areas as the CAHO document, and also stipulates that the site be indemnified for "the handling, use or subsequent transfer of Specimens and Genetic Data shipped by Site per Sponsor's instructions" (MAGI, 2011). The Medicines Australia's Form of Indemnity (Medicines Australia, 2011) and the UKCRC's Model Clinical trial Agreement for England only mention indemnification for subject injury.

Conclusion

The authors note clear evidence of an improvement in contract timelines since using the CAHO principles as a negotiating tool at their place of work (a not-for-profit academic hospital). Some sponsors have proactively used the principles in drafting templates to propose to sites. Templates aligned with the CAHO document have required little, if any, negotiation, and the authors' institution has been able to agree to such templates and implement them in under five business days from initial receipt. It is hoped that CAHO will eventually track negotiation timelines by asking for reports on this set of data from its member hospitals (Moldofsky et al., 2010).

There have been some challenges associated with the use of the standardized principles, mainly around interpretation of specific terms, by sites and industry sponsors alike. CAHO has considered the development of a glossary to address these issues. Another factor that has an impact on contract terms are policies and internal best practices, which differ among sites and are not transparent to sponsors. Sponsors have indicated frustration when these best practices appear more onerous. Also, some sites have reported inconsistently applying the principles, to the detriment of the message that they are the baseline standards. One sponsor interpreted the CAHO principles as guidelines and did not understand that all CAHO members had developed, agreed upon and committed to the parameters. In rare cases when sponsors have requested, and CAHO members have considered, exceptions to the principles, the institutions are encouraged to note the instances and forward them to CAHO. Future discussions will include a review of common areas of push-back from sponsors and

the resolution. Themes will evolve which could prompt clarification or a revision of certain positions. In addition, it must be noted that the CAHO Statement of Principles does not take the place of legal advice. The member hospitals are encouraged to use the document to establish satisfactory terms for their agreements and to seek legal counsel when appropriate (Moldofsky et al., 2010).

By developing a set of common principles for its member hospitals, CAHO provides a tool to effectively reduce the contract negotiation timeline in Ontario. Member hospitals are clear on the minimum standard contractual requirements for working with industry sponsors and sponsors have access to clear, consistent information among various sites. By creating this living document and making it available to both member hospitals and industry sponsors alike, both parties are able to quickly establish a common ground on the relevant ethical, legal and academic issues in a contract.

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