



Harmonization of Clinical Trial Agreements

Michelle Moldofsky

Karen Arts

Laurel Evans

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Agenda

- History of Ontario initiatives to standardize clinical trial agreements
- Introducing the CAHO initiative
- Purpose
- Status
- Elements of the Principles Document
- Purpose and use of the Best Practices Document
- Next steps
- Seeking input

We are representing the CAHO initiative, not our individual institutions.
We declare no financial conflicts of interest.



Introduction

- Why are we here?
- Background
- Process
- Principles document



Seeking the ultimate clinical trial agreement

- UK Model Agreement
- MAGI Model Agreement
- Other models?



Why does Canada need a different model?

- UK system is different from Canadian context
- MAGI model agreement challenges & status
- Negotiation timelines have become a serious barrier to conduct of research
 - Estimates go as high as 12 months per negotiation



Challenges to agreeing on content of clinical trial agreements

- Content
 - Issue identification vs. word-smithing
 - Tackle the principle & the words will follow
 - Harmonization with other organizations
 - Bargaining power
 - Negotiation strategies
- Development of a principles document



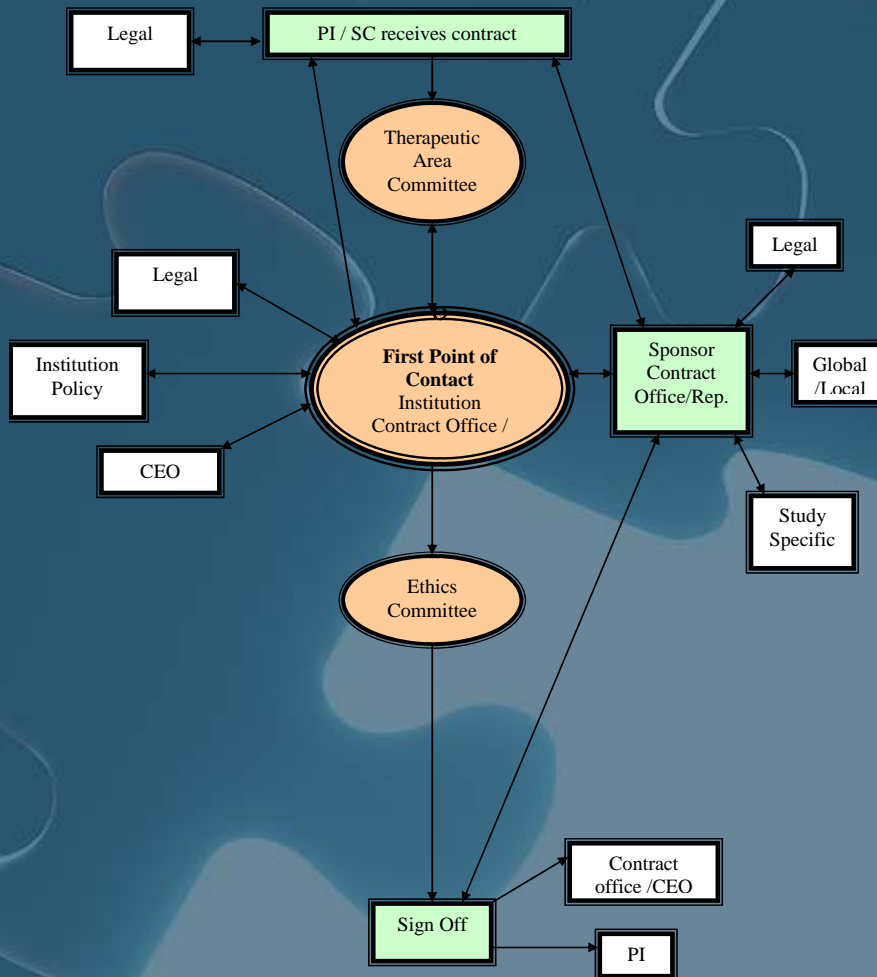
OICR Initiative

- OICR formerly Ontario Cancer Research Network (OCRN)
 - Industry, academic hospitals & community hospitals
 - Process & content working groups
 - Content stalled at point where needed to commit to principles



Agreement Process Map

Sample Process Flow for Routing Clinical Research Contract
(To be modified per institution to reflect your specific process)



OICR Initiative
Process Map,
Nov 2005



UofT Policy Harmonization

- **Clinical Study Agreements Working Group (CSAWG)**
 - A group of Toronto based hospitals
 - Had achieved harmonization of policies regarding clinical trial agreements at UofT*
- **Harmonization of policies at UofT**
 - Ability of companies to negotiate with multiple UofT-affiliated hospitals

*C.D. Naylor for the Research Committee and Clinical Study Agreements Working Group of the Toronto Academic Health Science Council, “Early Toronto experience with new standards for industry-sponsored clinical research: a progress report” 2002 CMAJ 166(4)



Council of Academic Hospitals of Ontario Initiative

- OICR content working group
 - Draft document with multiple choice principles
- CSAWG document
 - Principles used within UofT affiliated hospitals
- Council of Academic Hospitals of Ontario
 - 25 academic hospitals Ontario-wide
 - “Provides a focal point for strategic initiatives” – www.caho-hospitals.com
 - Draft principles document based on CSAWG document
 - Shared with member hospitals and with industry for comment



CAHO Steering Committee Members*

- **Arthur Slutsky**, Vice President, Research, St. Michael's Hospital; Chair
- **Michelle Moldofsky**, Manager, Contracts Office, The Hospital for Sick Children
- **Laurel Evans**, Business Services Coordinator, St. Michael's Hospital
- **Karen Arts**, Director Business Development, Ontario Cancer Research Network
- **Sarah Lampson**, Clinical Trial Agreements and Contracts Specialist, Hamilton Health Sciences
- Tamara Birkenheier, Research Contracts Specialist, Mount Sinai Hospital
- Paul Macpherson, Grants and Contracts Services, University Health Network
- Valerie Sales, Director, Clinical Studies Resource Centre, University Health Network
- Ron Heselgrave, Head, Research Ethics Board
- Deidre Henne, Director, Internal Audit and Research, Hamilton Health Sciences
- Marie Lynch, Chief Governance and Corporate Services and Chief Privacy Officer, St. Joseph's Healthcare Hamilton
- Sandi Machado, Manager, Grants and Contracts Office and Clinical Research Administration, Lawson Health Research Institute
- Marisa Akow, Director, Research Administration, Ottawa Health Research Institute
- Connie Day, Associate Vice President, Medical Administration, Credit Valley Hospital
- Samuel Ludwin, Vice President, Research Development, Kingston General Hospital
- Sharyn Szick, Administrative Director, University of Ottawa Institute of Mental Health Research
- Joe Gilbert, Vice President, Research, London Health Sciences Centre

*As of January 2007

****Bolding** indicates Working Group members.



Principles Document

- “Statement of Principles to be Considered When Negotiating a Clinical Studies Agreement”
- Purpose
 - Clear and up front about principles expected
 - Strategies of negotiation and issue identification matter
 - Seek consensus on the basics of a clinical trial agreement
 - Limit number of issues to negotiate



Elements of Principles Document

- Superior principles
- Publication
- Intellectual Property
- Confidentiality
- Privacy
- Indemnification
- Limitation of Liability of Institution/Investigator/No Warranties
- Disclosure of existence of contract & Use of name
- Parties' obligations
- Dispute resolution & governing law/jurisdiction
- Termination
- Additional Principles – for contracts with Contract Research Organizations



Superior Principles

- Study participants are volunteers offering themselves for human experimentation. Their safety must not only be, but must be seen to be, the overriding principle of the contract.
- All parties will comply with all applicable federal and provincial laws, regulations and Health Canada guidelines; with ICH GCP and the Declaration of Helsinki; and the parties to whom it is applicable will comply with the Tri-Council Policy Statement.



Superior Principles

- The study participants are drawn from the general public and have submitted themselves to experiment in good faith.
- The results, whether positive or negative, should be published within a reasonable time of completion of the study. The trial should be registered in a public registry (which meets the ICMJE criteria) in order to permit publication in peer-reviewed journals.



Conflict With UofT Principles

- Publication delay
 - 18 months (CAHO) vs. 12 months (UofT) for multicentre review
 - 2 months manuscript review + 2 months IP protection delay (CAHO) vs. 6 month review/delay (UofT)
- Outcome
 - UofT & its affiliated hospitals agreed in principle to adopt CAHO standard as its bottom-line



Other Principles

- Intellectual property
 - Context-specific component of any agreement
 - Both data and inventions may be owned by sponsor, institution or jointly by sponsor and institution
 - Negotiate on case-by-case basis
 - If owned by sponsor, institution/investigator to have rights for non-commercial, internal uses:
 - Administrative
 - Academic purposes
 - Research purposes
 - Study subject/clinical care purposes



Other Principles

- Confidentiality
 - Term must have an end date, not expected to be more than 10 years
 - Permitted disclosures include to potential study participants during the recruitment process or to study participants who are or were enrolled in the study, or their lawful representatives, in order to obtain and maintain informed consent or as the information relates to their health, safety or diagnosis



Other Principles

- Parties' Obligations
 - Adverse event reporting obligations and rights of Sponsor and Institution/Investigator to be set out
 - Includes, in event Sponsor fails to do so, right of Institution/Investigator to report SAEs and results required to protect the health of study participants directly to
 - regulatory authorities
 - data safety monitoring board
 - study participants or their lawful representatives
 - participating centres and their research ethics boards, and
 - applicable steering committee



Other Principles

- **Indemnification**
 - Some institutions will offer on behalf of Institution employees and agents only, excluding licensed physicians and their employees and agents
 - Investigators are not expected to provide an indemnification, but each may be asked to provide a statement accepting responsibility for his/her own actions and the actions of those for whom he/she is in law responsible.



Other Principles

- Note regarding Indemnification
 - Institution insurer (HIROC) and Investigator's defence provider (CMPA) have stated they will not cover for claims brought outside Canada. Institutions will have to make a risk management decision if institutions are asked to defend sponsor. Some Institutions won't agree to defend sponsors. If Institution does agree to defend sponsor as well as indemnify and hold harmless, Institution may indicate that Institution's obligation to defend applies within Canada only.



Steps to Implementation

- Seek buy-in from academic hospitals of Ontario
- Adopt as policy document & publish on web
- Use as negotiation tool
- Disseminate & request companies to use the document
- Quality assurance & tracking effectiveness
- Seek buy-in from community hospitals of Ontario
- Negotiate across Canada to develop a Canada-wide standard



Status of Implementation

- Principles document developed
- Input received from academic hospitals across Ontario
- Input received from 4 large pharma companies
- Input sought but not received from Ontario universities
- Principles document revised based on input
- Principles document agreed in principle by academic hospitals



Input Received

- Hospitals
 - 9 responses representing 7 hospitals
 - 4 agreed with documents as written
 - Other comments included:
 - Requests for clarification
 - Document modifications (adding items)
 - Conflict with UofT principles
 - Changes made with respect to:
 - Indemnification
 - Survival of rights



Input Received - Companies

- 4 responses representing 4 companies
- Positive about approach & quality of document
- 2 companies modified their templates (under negotiation)
- Comments included:
 - Requests for clarifications
 - Document modifications
 - Publication review timelines
 - (1 requested 6-9 mths instead of 120 days)
 - Indemnification



Input Received - Companies

- Concerns expressed regarding interpretation
 - Access to aggregate data
 - Disclosure of existence of contract & use of sponsor's name
 - Intellectual property rights (although these are flexible in document)
 - Record retention of confidential information
 - Privacy (which legislation is applicable)
 - SAE reporting only when sponsor fails to do so
- Changes made with respect to:
 - Indemnification (PI statement of liability)
 - Multiple clarifications



Best Practices Document

- “Clinical Trial Agreement Best Practices for Agreements with Private Industry Sponsors”
 - Complementary to Principles
 - Always in “draft” form
 - Internal document
 - Guidance document only
 - Not intended as legal advice



Why Best Practices Document?

- Variety of different individuals negotiating clinical trial agreements from varying backgrounds
- Size and sophistication of institutions varies widely
- Very little Canadian specific material to assist someone negotiating and/or reviewing these contracts
- Synthesis of experiences in negotiation by "seasoned" reviewers



Use of Best Practices

- Set up to mirror the Principles Document
- Best Practice vs. Acceptable vs. Not Acceptable
- Helps put Principles into Practice
- NOT to be used as, or intended as fundamental principles that can't be /shouldn't be abrogated.
- Guidance only, as to what is reasonable to ask for, what is reasonable to settle for



Next Steps

- Implementation at Ontario academic hospitals
- Present and publish principles
- Community hospital outreach
- Pharmaceutical company outreach
- Seek input from other Canadian jurisdictions regarding a Canada-wide standard



Seeking Your Input

- Implementation in Ontario
- Quality assurance mechanisms
- How to formulate a Canada-wide standard?



Contact Information

- Karen Arts
Director, Business Development
Ontario Institute for Cancer Research
karen.arts@oicr.on.ca, 416-673-6637
- Michelle Moldofsky
Barrister & Solicitor
miracle@ca.inter.net, 416-910-5763
- Laurel Evans
Director, Research Ethics
University of British Columbia
laurel.evans@ors.ubc.ca,