The proper clinical trial agreement that will protect Sponsors while negotiating with medical centers in Europe and USA

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The Clinical Trial

The Clinical trial is one of the most important stages in drug development processes.

The Purpose of the Clinical Trial is to ensure efficacy and safety of newly developed drugs.

Pharmaceutical companies are the most common sponsors of clinical trials.

Sponsors’ goal is to shorten the drug development stage in order to bring the drug to the global market in the most efficient way.

With changes in regulations and the acceptance by the regulatory authorities of clinical results from foreign countries Sponsors are taking the path of conducting international multi centers studies.
The Sponsored Clinical Trial Agreement

**Purpose:** To engage an institution and clinical investigator (PI) to conduct a sponsored clinical study. The agreement covers the legal rights of the parties in relation to the outcome of the clinical study.

- legal rights will be protected *only* after a *legally valid* agreement is signed or “executed”.

*Therefore any clinical trial* should be initiated and performed only after the execution of a legally valid Agreement.
When to start the legal negotiation process?

Finalizing the legal agreement is a time-consuming process – so when is the best time to initiate the negotiation process?

No definite answer can be given.

In some countries, the legal agreement is part of the regulatory submission process:

- Poland – a fully executed CTA is required for submission.

In others, the template agreement is required for submission but not the fully executed one:

- France
- Netherlands – approval of CTA language if in accordance with the CCMO guidelines.
- Belgium
When to start the legal negotiation process – Cont.

While in other countries the negotiation process to be initiated only after certain conditioned are met such as:

IRB/EC approval is obtained

Budget is finalized.

Sponsors should take proactive approach in order to expedite as much as possible the legal review process within the clinical sites.
The legal rights

The provision of the legal agreement:
• Conduct of the clinical study
• Confidentiality
• Intellectual property rights
• Rights and obligations of the parties in relation to the results generated in the course of the study
• Publication
• Insurance and Indemnification
• Termination
• Payment
The Non-negotiable provisions

Conduct the clinical study:
• In accordance with applicable laws and regulation including GCP and privacy laws.
• in compliance with the protocol
• Protection of study subjects (safety and private data protection)
• Sponsor right to have access to study documentation and records.
• Sponsor right to audit and monitor
• Secure the proper, use, storage and supervision of the study drug.
• Reporting of SAE including specific timelines.
• Study Staff
Confidentiality:

• All of Sponsor confidential information prior to the conduct of the study including Protocol, IB and information related to the study drug.

• Results generated in the course of the study including CRFs and other study reports.

• Study Subject personal information
Non negotiable Provision – Cont.

Intellectual Property rights (IP) –

• Retaining exclusive ownership rights to pre-existing IP
• Disclosure requirements
• Ownership rights to Study related IP –
  
  Inventions that relates to the study drug in the course of the conduct of the study such new uses and improvements to the study drug.
  
  Inventions that were conceived or reduced to practice by using the sponsor confidential information.
Non negotiable Provision – Cont.

- Publication:
  - Sponsor retain the first right to publish a multi study publication
  - Sponsor is the one to decide on authorship of the multi center publication.
  - Institution right to publish is subject to the following:
    - publication of results obtained at the institution only.
    - review by the sponsor prior to submission
    - sponsor’s right to remove any confidential information other than results
  Sponsor’s right to delay publication to protect IP
Termination:
Sponsor should have the right to terminate the agreement.
Institution should have only a limited right to terminate the agreement for safety – preferably IRB/EC decision of such need.

Post termination obligation of Institution to include:
Study subject safety
Final Study Reports
Budget and Compensation

The preferred terms to include

• Per patient detailed budget
• Payment for actual procedures performed
• Screen failure
• Standard of Care and subject insurance coverage
• Payment schedule to include last payment only upon conclusion, receipt of all data and reports including all quarries in relation to the study data.
Subject Injuries

Preferred terms

• Sponsor will reimburse institution only, for injuries that Sponsor Chief medical officer decides are drug related.
• Reimbursement for acute treatment costs only.
• No reimbursement if:
  • administration is not in strict adherence to the protocol.
  • injury is a results of negligence or deliberate act of PI or study staff.
  • Treatment would have been given to the subject in the ordinary course.
  • Injury is due to study subject pre-existing condition.
Inemnification

Preferred terms on behalf of the Sponsor*
Only for direct and study drug related injuries.
Not to be provided if the injury is a results of:
• PI or other staff member negligence or willful misconduct.
• Conduct of the study not in accordance with the protocol or applicable laws
• Breach of the terms of the agreement
* Not always negotiable

Standard Indemnity and Compensation Agreement (sICA) – Australia and NZ
• On behalf of the Institution*

usually terms will be reciprocal to the terms that deny indemnification – sponsor to be indemnified for injuries caused by:

PI or other staff member negligence or willful misconduct.
Conduct of the study not in accordance with the protocol or applicable laws
Breach of the terms of the agreement
* If allowed by law.

If no indemnity is provided – second best is a responsibility statement.
Insurance

Good practice: all sponsors should carry clinical trial/product liability/general coverage.

Many countries have specific insurance requirement which the sponsor must adhere.
Examples

- Belgium - No fault liability - strict liability for all events during the trial.
- Spain – required by law with strict liability
- Germany – required by law.
- UK – not required by law however in fact a proof of coverage is required.
- Israel – required by MOH guidelines.

Advice: always consult with a local broker to ensure the proper insurance coverage is obtained.
Use of Template Agreement

Objective:

• to develop a standardised Clinical Trial Agreement for use in contract clinical trials usually in consistent with international practice;
• to save time, money and manpower in order to facilitate the approval process;
• to have a streamlined contract negotiation process in order to reduce clinical trial start-up times;
• to ensure that the country remains an attractive location to conduct clinical research.
Template Use

Advantages to the Sponsor

• Single legal review by Sponsor is required of the contract for all centers to be utilized in the same country.

• Contracting process is de-risked for all contracting parties by having consistent contract terms with all clinical trial centers in the same country.

• Only budget and protocol specific requirements will need to be negotiated and reviewed.

• Sites are familiar with the contract therefore eliminating the need for a full review of contract, creating a streamlined and shorter period of contract negotiation process.
Template Use Disadvantage to the Sponsor

- If Agreement template is not to be modified or changed.
- Institutions, even if not forbidden from accepting modification, are reluctant to negotiate the agreement terms.
- Agreement terms are not consistent with the contract terms of other centers engaged in the conduct of the multi-center trial.
- Sponsor needs to be familiar with many type of agreement – more resources required by the sponsor in order to keep shorter negotiation process.
- Length of negotiation process is extended due to a strict review process for modifications.
Examples

- **France**: adopted on June 2014 Standard clinical trial agreement approach. This apply only to multi center studies and to governmental institution only. Amendments and modifications are not forbidden. Governmental institution to receive incentives for complying with the standard agreement approach.

- **Netherlands** – CCMO template – recommended but not a must. Amendments and modification as long as do not contradict the CCMO guidelines are permitted.

- **Belgium** – template exist but not a must.

- **UK** – Model Clinical Trial Agreement.

- **Australia** – adopted the Medicines Australia clinical research template. Changes are subject to approval by the Southern and Eastern Border States (SEBS) Committee. SEBS will consider contract amendments that are intended to accommodate, as far as possible, company-specific clauses that clarify or add to the CTRAs. Other modifications are not allowed.

- **New Zealand** Standardised Clinical Trial Research Agreement (sCTRA)

- **US** - The Clinical and Translational Science Award group (supported by NIH) developed and now implementing best practices in clinical research by using Accelerated Clinical Trial Agreement (ACTA). ACTA was accepted by 25 institution in US. Use of the template is on a voluntary basis.