Clinical Trial Agreements (CTA) Guidelines – advice from Qld Health Legal Unit

Table of Contents

1. Introduction ........................................................................................................... 2
2. Parties to the Contract ......................................................................................... 2
   Queensland Health ................................................................................................ 2
   Other Party ........................................................................................................... 2
3. Guidelines for use of the standard Clinical Trial Agreements (CTA).................... 3
   3.1 Commercially Sponsored CTA ...................................................................... 3
   Schedule 7 Special Conditions .......................................................................... 3
   Subcontracting Clause 20 ................................................................................ 4
   3.2 Corporate / Contract Research Organisation (CRO) CTA ......................... 4
   Schedule 7 Special Conditions .......................................................................... 5
   Subcontracting .................................................................................................... 5
   3.3 Collaborative Research Agreements (CRG CTA) ........................................ 5
   Schedule 4 Special Conditions .......................................................................... 6
   Subcontracting .................................................................................................... 6
4. Insurance ............................................................................................................ 6
5. Further information ............................................................................................ 7
1. Introduction

Queensland Health (QH) in collaboration with the Victorian Medical Insurance Authority (VMIA), interstate health departments, Medicines Australia (MA) and industry agencies have developed a set of uniformly accepted standard Clinical Trial Agreements (CTA’s).

Queensland Health has endorsed 3 standard CTA’s for use in Queensland Health institutions:
1. Commercially Sponsored CTA
2. Corporate Research Organisation (CRO) CTA
3. Collaborative Research Agreements (CRG) CTA


The use of the standard CTA’s will streamline the process of contract formation which must precede any research study commencing in QH. The terms contained in the body of the standard CTA’s must not be altered or amended in any way. Each of the standard CTA’s have a schedule where any particular operational requirements can be recorded as special conditions.

These Guidelines are intended to supplement the QH Research Management Policy & Framework 2008. This document provides further guidance on when the different standard CTA’s should be used and addresses a number of issues which have arisen in relation to the use of the standard CTA’s.

2. Parties to the Contract

The parties to a contract need to be properly identified to ensure that the correct legal entity is bound by the contract.

Queensland Health (QH)

The 'State of Queensland' is the contracting party for all QH agreements. The various state government departments (including QH) are not separate legal entities and cannot enter into contracts. Any wording which follows "The State of Queensland" is descriptive only and intended to assist the parties in identifying the relevant part/area/department within the State involved in the contract.

QH should be described on all research contracts as:
"The State of Queensland acting through Queensland Health (name of hospital/district) of (Address of Institution)".

Other Party

The other party to the contract may be a Sponsor, a CRO acting as a Local Sponsor, or a Collaborative or Cooperative Research Group (CRG). These parties may be various types of legal entities (eg proprietary company, company limited by guarantee, not-for-profit incorporated association, university or statutory body).

It is very important to independently verify the correct name and type of entity with whom QH is contracting, usually by doing an ASIC company search or other searches.
3. Guidelines for use of the standard CTAs

3.1 Commercially Sponsored CTA:

The Commercially Sponsored CTA is to be used where:
1. An Australian pharmaceutical company is sponsoring the trial; or
2. The Australian subsidiary of an international pharmaceutical company is sponsoring the trial.

The term 'sponsoring the trial' means taking overall responsibility for the conduct of the trial (i.e., initiates, organizes and supports a clinical study of an investigational product in human participants). This includes being the entity named on the Clinical Trial Notification (CTN) application and being the Sponsor party to the CTA which imposes obligations to (without limitation):
(a) liaise with the institution regarding the conduct of the trial and supply the investigational product;
(b) provide an indemnity in the form of the standard MA indemnity; and
(c) maintain insurance.

The Sponsor of the trial must be an Australian company or entity. The Sponsor will be the entity that endorses the Clinical Trial Notification (CTN) application.

Where the Sponsor is an international company or entity, the following options are available:

1. If the international company has an Australian affiliate, QH will contract directly with the Australian affiliate as the Sponsor using the Commercially Sponsored CTA; or

2. If there is no Australian affiliate, the international company may appoint a CRO to be responsible for the conduct of the trial in Australia (including acting as the Australian entity for the purposes of the CTN application), in which case the CRO CTA should be used naming the CRO as the Local Sponsor and the international company as the Organisation.

Schedule 7 Special Conditions

- Schedule 7 is to be used for the inclusion of Sponsor unique operational requirements that must be accommodated to allow for the conduct of the trial.
- Schedule 7 is not to be used to substantially amend the standard terms contained in the body of the CTA or to introduce additional clauses which contradict or otherwise undermine the substantial provisions and spirit of the standard CTA.
- QH (in conjunction with VMIA and NSW Health) has pre-approved a number of Schedule 7 requests from individual pharmaceutical companies for the Commercially Sponsored CTA.
- The approved Schedule 7 Special Conditions have been issued to both the Health Services and the respective pharmaceutical companies. A Commercially Sponsored CTA with a pharmaceutical company must only contain the Schedule 7 Special Conditions that have been issued to that pharmaceutical company as approved by QH. Any amendments or additions to these approved Schedule 7 Special Conditions proposed by a pharmaceutical company for a particular trial should be carefully considered and, if they involve legal issues, legally reviewed.

• If you would like to obtain a copy of the QH approved Schedule 7 clauses for a particular pharmaceutical company please contact the Research Ethics and Governance Unit – access is limited to QH district lawyers and Research Governance Officers.

• Where there is no approved Schedule 7 for a pharmaceutical company that QH is contracting with, any Schedule 7 Special Conditions proposed by that pharmaceutical company should be carefully considered and, if they involve legal issues, legally reviewed.

**Subcontracting Clause 20**

Clause 20 of the Commercially Sponsored CTA provides that the Sponsor may subcontract any of its obligations (save for the obligations regarding indemnity, insurance and compliance with compensation guidelines) in the Agreement. The Sponsor remains responsible for all subcontracted obligations and is liable for all acts and omissions of any subcontractor as if they were the Sponsor’s acts and omissions.

Clause 20 does not require the sponsor to notify the institution what obligations it has contracted out. This position was arrived at after lengthy negotiations with industry/MA. In situations where it becomes apparent to an institution that the Sponsor has subcontracted some of its obligations in relation to the trial:

- The institution should request from the Sponsor details of the name of the subcontractor and what obligations have been subcontracted (though the Sponsor is not contractually required to provide this); and
- The institution should maintain good communication and a close working relationship with the Sponsor to ensure it understands and has relevant information about what work that has been contracted out, in managing the trial.

There may be situations where there is an Australian company and a CRO involved in a trial. The manner in which these two entities allocate responsibilities for the conduct of the trial is a matter between them. However, it will be important for QH to identify which of the entities is to provide the MA indemnity, as this will determine which standard CTA is to be used.

- Where the Australian company is to provide the indemnity, the Commercially Sponsored CTA should be used naming the Australian company as the Sponsor. The Sponsor may then subcontract certain obligations (but not the obligation to indemnify, maintain insurance and comply with compensation guidelines) to a CRO.

- Where a CRO is to provide the indemnity, the CRO CTA should be used naming the CRO as the Local Sponsor and the Australian company as the Organisation.

### 3.2 Corporate / Contract Research Organisation (CRO) CTA

The CRO CTA is to be used when an international Organisation or an Australian company as owner of the investigational product engages a CRO to act as the Australian entity for the purposes of the CTN application. The CRO is then defined as
the Local Sponsor and assumes all responsibilities and obligations that attach to a Local Sponsor.

As the Local Sponsor, the CRO must:
- Provide the Medicines Australia Form of Indemnity
- Provide appropriate insurance. It is acceptable for the CRO to be a named additional insured under the International Organisation’s insurance policy – this will satisfy the obligation to provide appropriate insurance, provided the International Organisation’s insurance policy meets the specified level and coverage requirements.

**Schedule 7 Special Conditions**
- The standard terms of the CRO CTA should not be amended or altered in any way.
- The CRO CTA provides for any Special Conditions to be included in Schedule 7.
- There are no pre-approved Schedule 7 Special Conditions for the CRO CTA. Any Special Conditions proposed by a CRO should be carefully considered and, if they involve legal issues, legally reviewed.
- Schedule 7 is not to be used to substantially amend the CTA or to introduce clauses which contradict or otherwise undermine the substantial provisions and spirit of the Agreement.

**Subcontracting**
The CRO CTA does not include a clause in relation to subcontracting. If the CRO wishes to subcontract any of its obligations under the agreement, the parties may consider inserting a Special Condition in Schedule 7.

An example of a subcontracting clause is as follows:

*The Local Sponsor may subcontract any of its obligations under this Agreement, save for the obligations set out in clauses 5.1(8), 5.1(9) and 5.1(10) of the Agreement. The Local Sponsor remains responsible for all subcontracted obligations and is liable for all acts and omissions of any subcontractor as if they were the Local Sponsor's acts and omissions. The Local Sponsor must notify the Institution in writing the details of any subcontracting arrangements, including the name of the subcontractor and the nature of the subcontracted obligations. No subcontractor will have any rights under this Agreement against the Institution or be entitled to receive any payment from the Institution.*

3.3 **Collaborative Research Agreements (CRG CTA)**
The CRG CTA is to be used when a collaborative/cooperative group is the Sponsor of the clinical trial.

The CRG is defined as ‘an academic and/or non-commercial collaborative research group’. Technically only a legal person (e.g., an individual, company, incorporated association, statutory body) or a partnership of legal persons, can enter into and be bound by a contract. The kind of legal entity may depend on the circumstances of the research study. It will be particularly important when using this document to conduct the necessary searches to ensure that the correct legal entity is named as a party to the contract.
Referring merely to the name of the CRG will not sufficiently identify the correct legal entity. For example, a co-operative research centre (CRC) typically has an incorporated CRC company that enters into contracts for the CRC – that company is likely to be the appropriate party to the contract. If a research group resides within a research or educational institution, the institution may be the appropriate contracting party. If there are a number of institutions in a CRG, there may be one lead institution entering into the contract on behalf of the others, or each of the institutions may enter into the contract together.

There may be studies or research projects involving academic or non-commercial collaborative research groups that are not in the nature of a clinical trial. The CRG CTA should not be used in those circumstances. Please refer to Implementation Standard 4, Section 17 ‘Non-Standard Study Agreement’ of the QH Research Management Policy & Framework 2008.

**Schedule 4**
- The standard terms of the CRG CTA should not be amended or altered in any way.
- The CRG CTA provides for any Special Conditions to be included in Schedule 4.
- There are no pre-approved Schedule 4 Special Conditions for the CRG CTA. Any Special Conditions proposed by a CRG should be carefully considered and, if they involve legal issues, legally reviewed.
- Schedule 4 is not to be used to substantially amend the CTA or to introduce clauses which contradict or otherwise undermine the substantial provisions and spirit of the Agreement.

**Subcontracting**
The CRG CTA does not include a clause in relation to subcontracting. If the CRG wishes to subcontract any of its obligations under the agreement, the parties may consider inserting a Special Condition in Schedule 4.

An example of a subcontracting clause is as follows:

*The CRG may subcontract any of its obligations under this Agreement. The CRG remains responsible for all subcontracted obligations and is liable for all acts and omissions of any subcontractor as if they were the CRG’s acts and omissions. The CRG must notify the Institution in writing the details of any subcontracting arrangements, including the name of the subcontractor and the nature of the subcontracted obligations. No subcontractor will have any rights under this Agreement against the Institution or be entitled to receive any payment from the Institution.*

**4. Insurance**
The Commercially Sponsored CTA and the CRO CTA both require the other party to have and maintain insurance with respect to its activities under the CTA’s (refer to clauses 5.1(8) and 5.1(10) respectively). The insurance requirements must be stated in Schedule 4.

The requirement to maintain insurance is a very important contractual obligation, however the clause will have no effect unless Schedule 4 is completed properly.
The type and level of insurance required for each agreement will depend to some extent on the level and nature of the risks involved with the study. However, as a general guideline QH should include the following insurance requirements in Schedule 4:

The Sponsor/Local Sponsor must have and maintain for the term of this Agreement and for a period of 6 years thereafter the following insurances:

(a) Clinical Trial/Product Liability insurance for an amount not less than $10m per claim;

(b) Public liability insurance for an amount not less than $10m per claim;

(c) Professional indemnity insurance for an amount not less than $10m per claim;

(d) Workers compensation insurance in accordance with applicable legislation.

For all QH CTA’s please delete the current wording in Schedule 4 which relates to Victorian specific insurance requirements.

The requirement to maintain insurance for 6 years following completion of the study is intended to ensure that insurance will be available in the event that a claim is made after the trial has finished. Adverse health outcomes for patients often do not present immediately, however personal injury proceedings must be commenced within a 3 year time limitation. Any proceedings based on breach of contract are subject to a 6 year time limitation.

It is recommended that you seek legal advice if you intend to include insurance requirements in Schedule 4 different from those specified above.

5. Further Information

If you require further information or assistance regarding the use of the standard CTA’s please contact the Research Ethics and Governance Unit 07 323 40034.