Clinical Research Agreement Guidelines

1. Introduction

Each clinical trial to be conducted at a site within SA Health and sponsored by a third party external to SA Health must be governed by a written agreement clarifying the obligations and responsibilities of the parties involved in the trial.

The CALHN Research Office recommends that standard clinical trial/investigation agreements are used for clinical research studies, as this will streamline the process of contract negotiation which must precede any clinical research study commencing in SA Health.

1.1. Medicines Australia Agreements

Commercially Sponsored studies CTRA:
For commercially sponsored studies where the company has accepted all the roles of the sponsor the "Clinical Trial Research Agreement Medicines Australia - Standard Form" should be used.

Contract Research Organisation CTRA:
Where the Contract Research Organisation (CRO) has accepted all the roles of the sponsor the "Clinical Trial Research Agreement Medicines Australia CTRA: Contract Research Organisation acting as the Local Sponsor" should be used.

Collaborative Group Sponsored CTRA:
In the case of a collaborative sponsored clinical trial, the "Clinical Trial Research Agreement Collaborative or Cooperative Research Group (CRG) Studies - Standard Form" should be used.

Phase IV CTRA:
For post marketing surveillance Phase IV studies the "Clinical Trial Research Agreement-Phase 4 Clinical Trial (Medicines)" should be used.

These documents are available on the Medicines Australia (MA) website:
http://medicinesaustralia.com.au/issues-information/clinical-trials/clinical-trials-research-agreements/

1.2. Medical Technology Association Of Australia Agreement

Commercially Sponsored Device Trial CIRA:
For commercially sponsored device trials the "The MTAA Standard Clinical Investigation Research Agreement - Standard Form" should be used:

This document is available on the Medical Technology Association of Australia (MTAA) website: http://www.mtaa.org.au/policy-initiatives/clinical-investigations

1.3. Investigator Initiated Agreements

Non-commercial clinical trials
There are no template agreements for trials that are investigator initiated or collaborative studies, and as such, each agreement will require review by the CAHLN Research Office.

2. Parties To An Agreement

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

"**Central Adelaide Local Health Network Incorporated (ABN 96 269 526 412)**" is the legal entity for all CALHN research agreements.

This includes research agreements with the Royal Adelaide Hospital, The Queen Elizabeth Hospital and SA Pathology which are not separate legal entities, and cannot enter into contracts.

Any wording which follows "**Central Adelaide Local Health Network Incorporated (ABN 96 269 526 412)**" is descriptive only and intended to assist the parties in identifying the relevant organisation/site within CALHN that is involved in the contract.

Please note: The use of this extra wording is not necessary as the organisation/site is listed in Schedule 1 of the MA and MTAA Clinical Trial Agreements.

Please refer to the document "Parties and Signatories to a CALHN Research Agreement" at http://www.rah.sa.gov.au under the "Research" tab.

3. Commercially Sponsored Research Agreements

3.1. Commercially Sponsored Drug Study Agreement:

The "Clinical Trial Research Agreement Medicines Australia - Standard Form" should be used where:

a) The study is initiated by an Australian pharmaceutical / biotechnology company sponsoring the clinical trial; or the Australian subsidiary of an international pharmaceutical/biotechnology company ("Commercial entity") and not by a SA Health investigator.
b) The commercial entity is the sponsor for the purposes of the CTN/CTX Scheme.
c) The clinical trial is conducted to investigate a drug/biological for commercial exploitation by its manufacturer/sponsor.
d) The protocol has been developed and is the responsibility of the commercial entity.
e) Intellectual property developed as a result of the clinical trial is owned by the relevant commercial entity.

The term 'sponsoring the clinical trial' means taking overall responsibility for the conduct of the trial (ie initiates, organises and supports a clinical study of an investigational drug / biological in human participants). This includes:

a) liaising with the Institution regarding the conduct of the trial
b) supplying the investigational drug / biological;
c) providing an indemnity in the form of the standard Medicines Australia indemnity agreement; and
d) maintains insurance throughout the trial.

The parties to the agreement are:

The 'Institution', which is CALHN

The 'Sponsor', which is the commercial entity sponsoring the clinical trial.

The 'Sponsor' must be an Australian entity because, among other reasons, the 'Sponsor' is the sponsor for the purpose of the CTN/CTX Scheme and the 'Sponsor' must provide an indemnity (in the appropriate form) in favour of CALHN. These are obligations that must be performed by an Australian entity.

The ‘Principal Investigator’, though named in Schedule 1 to the agreement, is not a party to the CTRA. However, the Principal Investigator may sign the agreement to acknowledge the obligations it imposes.

The agreement may be amended by inserting ‘Special Conditions’ into Schedule 7 of the Agreement. See section 5 of this document.

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

a) If the international company has an Australian affiliate, CALHN will contract directly with the Australian affiliate as the Sponsor using the Commercially Sponsored CTRA; or
b) 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 CTRA should be used naming the CRO as the Local Sponsor and the international company as the Organisation.

3.2. Commercially Sponsored Device Study Agreement:

“The MTAA Standard Clinical Investigation Research Agreement - Standard Form” should be used where:

a) The study is initiated by an Australian medical device company sponsoring the clinical investigation; or the Australian subsidiary of a medical device company and not by a SA Health investigator.
b) The medical device company is the sponsor for the purposes of the CTN/CTX Scheme.
c) The clinical investigation is conducted to investigate a medical device for commercial exploitation by its manufacturer/sponsor.
d) The clinical investigation plan has been developed and is the responsibility of the medical device company.
e) Intellectual property developed as a result of the clinical investigation is owned by the relevant medical device company.

The medical device company is the Sponsor of the Clinical Investigation and

a) liaises with the Institution regarding the conduct of the trial
b) supplies the medical device;
c) provides an indemnity in the form of the standard Medical Technology Association of Australia indemnity agreement; and
d) maintains insurance throughout the investigation.

The parties to the agreement are:

The ‘Institution’, which is CALHN

The ‘Sponsor’, which is the medical device company sponsoring the clinical investigation. The ‘Sponsor’ must be an Australian entity because, among other reasons, the ‘Sponsor’ is the sponsor for the purpose of the CTN/CTX Scheme and the ‘Sponsor’ must provide an indemnity (in the appropriate form) in favour of CALHN. These are obligations that must be performed by an Australian entity.

The ‘Principal Investigator’, though named in Schedule 1 to the agreement, is not a party to the CIRA. However, the Principal Investigator may sign the agreement to acknowledge the obligations it imposes.

The agreement may be amended by inserting ‘Special Conditions’ into Schedule 7 of the Agreement. See section 5 of this document.

3.3. Corporate / Contract Research Organisation (CRO) CTRA

The "Clinical Trial Research Agreement Medicine Australia CTRA: Contract Research Organisation acting as the Local Sponsor" agreement should be used when an international organisation or an Australian company as owner of the investigational product engages a Contract Research Organisation (CRO) to act as the Australian entity for the purposes of the CTN application.

The CRO assumes all responsibilities and obligations that attach to a local sponsor of a commercially sponsored clinical trial. This includes providing:

a) An indemnity in the form of the standard Medicines Australia indemnity agreement; and
b) Appropriate insurance. It is acceptable for the CRO to be a named as 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.

The parties to the agreement are:

The 'Institution', which is CALHN

The 'Local Sponsor' is the commercial entity sponsoring the clinical trial.

The 'Local Sponsor' must be an Australian entity because, among other reasons, the 'Local Sponsor' is the sponsor for the purpose of the CTN Scheme and the 'Local Sponsor' must provide an indemnity (in the appropriate form) in favour of CALHN. These are obligations that must be performed by an Australian entity.

The 'Principal Investigator', though named in Schedule 1 to the agreement, is not a party to the CTRA. However, the Principal Investigator may sign the agreement to acknowledge the obligations it imposes.

The agreement may be amended by inserting 'Special Conditions' into Schedule 7 of the Agreement. See section 5 of this document.

3.4. Phase IV Clinical Trial (Medicines)

The "Clinical Trial Research Agreement Phase 4 Clinical Trial (Medicines)" should be used for post marketing surveillance Phase IV studies.

The Sponsor is responsible for initiating, managing, developing and coordinating the clinical trial. There is no requirement under the agreement for a sponsor to provide an Indemnity or evidence of its insurance arrangements for Phase IV studies.

The parties to the agreement are as follows:

The 'Institution', which is CALHN

The 'Sponsor' is the commercial entity sponsoring the clinical trial.

The 'Sponsor' must be an Australian entity because, among other reasons, the 'Sponsor' is the sponsor for the purpose of the CTN/CTX Scheme and the 'Sponsor' must provide an indemnity (in the appropriate form) in favour of CALHN. These are obligations that must be performed by an Australian entity.

The 'Principal Investigator', though named in Schedule 1 to the agreement and is not a party to the CTRA. However, the Principal Investigator may sign the agreement to acknowledge the obligations it imposes.

The agreement may be amended by inserting 'Special Conditions' into Schedule 4 of the Agreement. See section 5 of this document.

4. Non Commercial Research Agreements

4.1. Collaborative Research Agreements (CRG CTRA)

The "Clinical Trial Research Agreement Collaborative or Cooperative Research Group (CRG) Studies - Standard Form" 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'. 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.

The CRG is responsible for initiating, managing, developing and coordinating the clinical trial. There is no requirement under the CRG CTRA for a CRG to provide an Indemnity or evidence of its insurance arrangements. However, it is recommended and if a CRG incorporates such provision into the CTRA, or otherwise offers such Indemnity, it would be prudent for CALHN to accept that indemnity.

The parties to the CRG CTRA are as follows:

The 'Institution', which is CALHN

The 'CRG' is the collaborative or cooperative research group that is the sponsor of the clinical trial. The 'Sponsor' must be an Australian entity because, among other reasons, the 'Sponsor' is the sponsor for the purpose of the CTN / CTX Scheme and the 'Sponsor' must provide an indemnity (in the appropriate form) in favour of CALHN. These are obligations that must be performed by an Australian entity.

The 'Principal Investigator', though named in Schedule 1 to the CRG CTRA, is not a party to the CTRA. However, the Principal Investigator may sign the CRG CTRA to acknowledge the obligations it imposes.

The agreement may be amended by inserting 'Special Conditions' into Schedule 4 of the Agreement. See section 5 of this document.

4.2. Investigator Initiated Research Agreements

For trials that are investigator initiated or collaborative studies there is no current template agreement and as such each agreement will require review by the CALHN Research Office.

4.3. International Research Agreements

CALHN Organisations may also undertake clinical trials in collaboration with non-commercial overseas or international partners such as universities, research institutes and collaborative groups who do not have any representation in Australia.

These trials may be investigator initiated or collaborative group studies where each Australian participating site acts as its own 'sponsor' for the purposes of the CTN notification to the TGA.

CALHN Organisations will generally need to enter directly into a clinical trial agreement or research collaboration agreement with the international partner. The agreements will usually be on international templates which are not part of the suite of standard CTRA agreements.

The CALHN Research Office should be contacted in respect of such international agreements to ensure they do not contain clauses that are contrary to the SA Health's

Insurance Requirements or clauses that impose additional indemnities on parties to the agreement.

5. Special Conditions To An Agreement

The terms contained in the body of the standard agreements must not be altered or amended in any way. Any minor amendments that may be required to accommodate any operational requirements of either party can be made through Schedule 7 (or Schedule 4 of the CRG and Phase IV MA CTRAs).

The CALHN Research Office reviews the agreements and has a number of approved Schedule 7 provisions submitted by individual sponsors for the CTRA/CIRAs.

In addition, SA Health now participates in a multi-jurisdiction review group to consider amendments to the standard agreements called the Southern and Eastern Border States (SEBS) review group.

A process is outlined in the document "SEBS Schedule 7 and 4 Special Conditions to an Agreement" at http://www.rah.sa.gov.au under the "Research" tab.

The SEBS review group meets monthly to consider CTRA/CIRA amendments.

6. Review Of Clinical Research Agreements

The Clinical Research Agreement must be reviewed and submitted to the CALHN Research Office as part of the application for Site Specific Assessment. Please refer to the "Full Site Specific Assessment" at http://www.rah.sa.gov.au under the "Research" tab.

Any queries should be made to the CALHN Research Office on 8222 3839 or via email at Health.ResearchGovernanceIP&Contracts@sa.gov.au