



Clinical Trials Business Unit (CTBU) CLINICAL TRIAL INFORMATION FOR EXTERNAL PARTIES

Royal Perth Hospital (RPH) has a proud tradition of actively participating in clinical trials, operating on the principle that a strong clinical research foundation enhances the delivery of high quality clinical care. In response to the Western Australian (WA) Government's recommendations for greater accountability in the conduct of research activities, RPH established the Clinical Trials Business Unit (CTBU). The CTBU mission is to provide world best practice in the governance of all Commercial and Non-Commercial clinical trials (legal, financial, indemnity, insurance), as well as fostering RPH as a centre of excellence in clinical research.

CLINICAL TRIAL GOVERNANCE

Clinical Trial Governance Approval

Clinical Trial Applications for all new, extension and contractual amendments to Commercial and Non-Commercial trials at RPH must go through two processes of clinical trial governance approval involving ethical review by the RPH Human Research Ethics Committee (HREC) AND clinical trial governance by the CTBU before commencement. These approvals can take place separately and concurrently as the two departments operate independently. **Approval letters from both the HREC Chair and CTBU Business Development Manager, must be received by the Principal Investigator before a trial can proceed.**

Human Research Ethics Committee (HREC)

The RPH Ethics Committee is responsible for the ethical review of human research and clinical trials, involving initial, extension and reciprocal approval projects. This involves the review of the processes, Protocol, related product (CTN/CTX Forms) and patient information and consent documentation. The HREC will only liaise with the Principal Investigator and will not enter into negotiations with external parties, therefore the PI or Trial Coordinator (TC) should be contacted to facilitate the HREC application.

Clinical Trials Business Unit (CTBU)

The CTBU is administered by the Business Development Manager, Katherine Coltrona and Research Governance Officer, Bonnie McLeod and is responsible for the legal, financial and liability governance of clinical trials. This involves the review of all contractual, financial, indemnity and insurance documentation to ensure compliance with laws, regulations and codes of practice.

Following the initial CTBU application from the PI, the submission will be assigned a CTBU number. Submissions are processed in chronological order and once the trial review is initiated the CTBU will liaise with the PI, TC, Sponsor and/or Collaborative Research Organisation (CRO), to review, negotiate and approve the Clinical Trial Research Agreement, Indemnity, Insurance and Financial documentation for each clinical trial. Enquires are welcome but documentation will not be reviewed until the submission review is activated by one of the Governance Officers. This process has been adopted to prevent delays to prior applications currently under review.

Enquires to: CTBU ☎ +61 8 9224 2260 📧 RPH.CTBUadministration@health.wa.gov.au

✉ Level 5, Colonial House, RPH, Wellington St. Perth, WA, 6000.

Clinical Trial Business Unit Office hours: Monday – Friday 9.00am - 5.00pm.



Reciprocal Agreements

The RPH HREC has a reciprocal agreement with the Ethics Committees of University of WA (UWA), Fremantle Hospital (FH) and Sir Charles Gairdner Hospital (SCGH). Clinical Trials that are granted ethical approval by these Institutions are accepted by the RPH Ethics Committee and go through a less exhaustive review, facilitating a speedier review process.

The CTBU does not have a reciprocal governance approval system in place, so all trials receive the same comprehensive review and thus cannot be fast tracked. The Governance Units of RPH, FH, SCGH however do have a reciprocal agreement with the WA Department of Health, the State Solicitors Office and Insurance Commission of WA (RiskCover) and will accept Clinical Trial Research Agreements (CTRA) negotiated with from these Institutions; facilitating a speedier review process of legalities and Insurance. RPH CTBU has already negotiated many CTRA templates with pharmaceutical companies and Collaborative Research Groups (CRG) on behalf of the WA Public Sector Hospitals.

CONFIDENTIALITY AGREEMENTS (CDA)

The State Solicitor's Office of WA recommends that public sector employees do not sign confidentiality agreements if they are required at the outset of clinical trial discussions. Public sector employees are required by the Public Sector Management Act 1994 to keep information obtained in the course of their employment confidential. Under section 81 of the Criminal Code of Western Australia unauthorised disclosure of information is a criminal offence punishable by up to 3 years imprisonment. Accordingly confidential information provided to a public sector employee is more than adequately protected by law.

If a CDA is still required, a ***RPH Confidentiality Agreement Template*** has been produced by the State Solicitor, to reduce the legal time required to review each Sponsor's/CRO's individual *Confidentiality Agreements*. The PI will forward this template to the Sponsor/CRO during the initial correspondence regarding a trial. CTBU will negotiate and process the agreements for the Director of Clinical Services to sign on behalf of the Institution which is effective for 5 years. The PI does not have the legal jurisdiction to sign on behalf of the Institution and its employees. The CTBU maintains a record of the CDA executed with external parties and (if these are not trial specific) are available to cover all future trials for the 5 year period. A copy of this will be forward to the interested parties involved.

CTBU CLINICAL TRIAL APPLICATIONS

On commencement of clinical trial negotiations the CTBU is available to provide advice on the appropriate governance documentation (Clinical Trial Research Agreement, Indemnity and Insurance) and fees, both to Researchers and to External Parties.

The initial budget should be negotiated by the PI and Sponsor. As part of financial governance, the PI is responsible for conducting an internal financial review of costs for their Department, Service Departments, CTBU and RPH infrastructure in comparison to external funding. When the CTBU has received a Clinical Trial Application and commenced the review process it is available to assist with the negotiation of fees, additional remuneration, and negotiate the CTRA, Indemnity Form and insurance directly with the external parties whilst keeping the PI/TC copied into negotiations.

A CTBU Clinical Trial Application should be submitted as soon as the documentation is available as approvals can take between 6 weeks to 3 months. This application can occur prior to or at the same time as the HREC Submission as the two review processes occur independently of each other and require different documentation. To facilitate the review process, CTBU recommends that Sponsors/CRO provide the following relevant documentation in electronic format. It is advisable not to send hard copies of signed documents prior to CTBU approval as they may require amendments:

1. *Protocol.*
2. *Clinical Trial Research Agreement (CTRA)*
3. *Sponsor's Budget and Payment Schedule*
4. *Medicines Australia (MA) Form of Indemnity*
5. *Insurance Certificate of Currency +/- Policy*



LEGAL AGREEMENTS

Legal Entity

Organisations entering into a *Clinical Trial Research Agreement (CTRA)* must be legal entities; therefore the CTRA must identify and define their legal title (including ACN/ABN), registered address and business name. The commercial external parties, e.g. Sponsor or Contract Research Organisation (CRO), should be incorporated within Australia, or for the purposes of an agreement with the Institution, use a subsidiary that is incorporated within Australia.

(NB: Electronic signatures are not acceptable on legal documents)

RPH as the Institution is not a legal entity in itself and thus the title on all legal documentation (*Clinical Trial Research Agreements, Indemnity and CTN/CTX Forms*) should read:

The Minister for Health is incorporated as the board of Royal Perth Hospital (ABN 13 993 250 709) of Wellington St, Perth, WA 6000, under s7 of the Hospitals and Health Services Act 1927 (WA) and has delegated all the powers and duties as such to the Director General of Health.

(NB: On CTRA and CTN Forms the address and ABN may be removed and documented below in the appropriate place.)

The signatory on legal documentation should read:

Signed on behalf of the Institution, for and on behalf of the Director General of Health as delegate of the Minister for Health, by its duly authorised representative.

(NB: this signatory must be included in the MA Form of Indemnity)

The standard CTRA recognises the Principal Investigators responsibility for the conduct of the study, but they do not have authority on behalf of the Institution to sign or amend the *CTRA* or the *Protocol*. **All legal agreements must be signed by the appointed representative of the Minister for Health, including Amendments, CTN/CTX, Pharmacy and Imaging Agreements and Indemnity Forms.**

Clinical Trial Research Agreements

RPH has adopted the Standard ***Medicines Australia Clinical Trial Research Agreement (CTRA)*** and ***Medicines Australia Indemnity Form*** formulated by Medicines Australia and WA Department of Health for use in all clinical trials involving external parties. **The Department of Health, State Solicitors Office and RiskCover** has made several changes in Schedule 7 to the standard Medicines Australia Clinical Trial Research Agreement. These changes reflect WA Government law as well as ensuring the rights of the Institution, PI and subject is protected. The CTBU will negotiate these changes with both Commercial and Non-Commercial entities until a mutually agreeable contract is finalised. Templates are available from the PI/TC for the following:

Commercially Sponsored Trials

RPH (as delegate of the Minister for Health) and the Commercial Trial Sponsor +/- CRO:

- 1. Commercial Bipartite Clinical Trial Research Agreement** - The "***Clinical Trial Research Agreement – Medicines Australia Standard Form***" is used by WA Health where the parties to the agreement are the Minister for Health (delegate) and the Sponsor. The Sponsor is either the commercial entity sponsoring the trial, or a CRO, contracted by the commercial entity to undertake the Sponsor's role. If the Sponsor is not party to the agreement, the CRO must provide the indemnity and insurance; it can not provide indemnity as an agent of the Sponsor.
- 2. Commercial Tripartite Clinical Trial Research Agreement** - The "***Clinical Trial Research Agreement –Standard Form B***" applies to a Clinical Trial involving three parties, specifically the Minister for Health (delegate), a Sponsor and a CRO.

Non-Commercial Clinical Trials

RPH (as delegate of the Minister for Health) and a Non-Commercial external party:

- 1. Non-Commercial Clinical Trial Research Agreement for Cooperative Research Groups (CRG)** applies to Clinical Trials where the Minister for Health (delegate) enters an agreement with a Non-Commercial CRG.



Clinical Trials carried out at RPH require either 3 or 4 original copies of any legal document to be signed; these copies are for the following:

1. Institution – retained by CTBU
2. Principal Investigator – retained by Trial Department
3. Sponsor – retained by Sponsor
4. CRO – retained by CRO

NB: As the MA Form of Indemnity is a Schedule of the CTRA the same number of final copies is required as the CTRA.

Amendments

All Amendments (Budget or Legal) or Addendums to the Clinical Trial Research Agreement must be reviewed by the CTBU and signed by the Director of Clinical Services as the representative of the Minister for Health. The PI does not have the authority to sign these on behalf of the Institution.

INDEMNITY

In Commercially Sponsored Trials, an indemnity is required either from the Sponsor or CRO in the format of the *Medicines Australia Form of Indemnity*. When the Sponsor is an overseas entity and party to the CTRA, the indemnity may be provided by the Sponsor or by the representative CRO. This Agreement will indemnify the hospital and its employees against claims arising from the study (the Indemnity covers the RPH HREC so it does not require a separate contract). Should an allegation of negligent conduct by the PI or the Institution be made; employees working on clinical trials are indemnified under a WA State Government policy that covers, employees acting in good faith and in accordance with the terms of their employment. A ***RPH Medicines Australia Form of Indemnity Template*** is available from the PI/TC.

(NB: The legal titles on the Indemnity Form must match the CTRA i.e. if the party is named as a CRO in the CTRA they should be named as CRO in the title and body of the Indemnity Form.)

INSURANCE

In Commercial Trials the Sponsor and CRO are required to effect and maintain insurance to cover the Sponsor's/ CRO's liabilities which may arise in respect to the Study, by means of:

- Product liability insurance for a minimum sum insured of AUD \$10,000,000 and also in the aggregate;
- Public liability insurance for the minimum sum insured of AUD \$5,000,000; and
- Liability insurance covering the liabilities of the Sponsor or the CRO for a minimum sum insured of AUD \$10,000,000 and also in the aggregate.

As a prerequisite for a Clinical Trial to commence, the *Insurance Certificate of Currency* must be provided to the CTBU as evidence of the Sponsor's / CRO's insurance, and the terms be acceptable to cover the *Clinical Trial, Product and Public liabilities*. A CRO not party to the CTRA will still have to provide evidence of Public Liability Insurance if they wish to conduct business on the RPH site. For insurance companies based in Australia [and listed on the Australian Prudential Regulation Authority's (APRA) list of acceptable insurers], in most cases the certificate of currency is an acceptable evidence of cover. Extreme care should be taken with "No Fault Compensation" policies as they may remove the rights of subjects to common law claims. Those with cover listed as "No Fault Compensation" must provide further evidence of "legal liability" cover.

Issues arise with an ***Overseas Insurance Policy i.e. not APRA approved***; the cover wording of the policy is required to assess the veracity of the policy by RiskCover. Although the insurance industry uses common terms to describe the various classes of insurance, the actual policies offered by insurers within each class can vary significantly and the wording of the overseas policies may not always be clear. If the Sponsor is unable to provide the policy wording the following information must be provided:

- Name and address of the insurer, including its Internet website address.
- Name and address of the insured.
- Policy number.
- Period of insurance.
- Class of insurance.
- Sum insured per event. Include any sub limits.
- Aggregate sum insured.
- If applicable, any excess of loss/umbrella policy information.
- Deductibles/excesses.



- Whether the policy is constructed on “occurrence” or “claims made” wording. If the latter, there is a further requirement for the sponsor to maintain continuous insurance for 6 years after conclusion of the Clinical Trial. This can be achieved using different insurers and different insurance policies.
- Scope of cover. For example, “Legal liability of the insured for death and bodily injury arising from Clinical Trials, including products liability risks”. There may be a need to quote the operative clause of the policy to capture the correct interpretation.
- Territorial limits of the policy are there are any restrictions on claims in an Australian jurisdiction.
- Relevant policy exclusions and conditions should be listed and detailed if appropriate. Exclusions relating to specific drug use or implements may be important

In Non-Commercial Trials RPH (as delegate for the Minister for Health) may assume the risk of the trial, provided a risk assessment is made by the CTBU. Should a civil claim arise as a consequence of the trial, the State Government’s indemnity arrangements mean that RiskCover (which manages the self-insurance arrangements for WA Health), will generally be relied upon to meet the costs of responding to that claim.

FINANCE

Fees

The RPH Clinical Trial Fees are outlined in the *CTBU Clinical Trial Fees* Document which can be obtained from the PI or CTBU. **RPH does not charge Ethics Fees** the costs involved in RPH clinical trial governance are covered by the Clinical Trial Application Fee (CTAF) which is applied to all Commercial Trials and invoiced directly by the CTBU and must be paid irrespective if the trial commences or the CTRA is executed.

The CTRA Payment Schedule should contain the following information

- ❖ Payment amounts
- ❖ Payment regularity and time interval
- ❖ Invoicing method – Tax invoice or Recipient Created Invoice
- ❖ Payment method – cheque, credit card, EFT
- ❖ Payee details(Debtor)
- ❖ Recipient details (Health Corporate Network or Trial Coordinators Details)
- ❖ Payments of Service Departments

RPH has created a Payment Details table in the CTRA Schedule 2 to document the above details.

Invoicing & Payments

Invoicing for clinical trials can occur either by direct invoice or recipient created tax invoice (RCTI). RPH utilises the services of **Health Corporate Network (HCN)** for raising invoices. HCN will send the external party a tax invoice with the relevant trial information and payments instructions.

Payment of remuneration by cheque or credit card is preferred. The payment by **Cheque or Credit Card** should be made payable to **SMAHS Royal Perth Hospital** and sent with the remittance directly to the **HCN** at the address on invoice – **PO Box 8549 Perth Business Centre WA 6849**. Electronic Fund Transfer (EFT) is acceptable, but is discouraged as it is often harder to track funds if the payee does not supply the correct payment details. If paying by EFT the payee should notify the HCN/TC and send the remittance advice to HCN.FA@health.wa.gov.au

Service Departments

The RPH Pharmacy and Imaging Departments can either charge their fees as part of the CTRA and invoice through the Trial Department **or** deal directly with the Sponsor using a separate **Pharmacy/Imaging Financial Agreement**, in the latter no Pharmacy/Imaging Fees are documented in the payment schedule but will be documented in an appendix to the CTRA and invoiced to the Sponsor independently. **This Pharmacy/Imaging Financial Agreement is reviewed by the CTBU as it will form an Appendix to the CTRA and be signed by the Director of Clinical Services.**

Goods & Services Tax (GST)

All costs are subject to GST (10%) if the Sponsor is registered as an entity in Australia. An overseas Sponsor is NOT subject to paying GST as RPH is supplying the results of the trial to a party not located in Australia.