Clinical Trials Procedure

Version 3 – Approved 16 October 2024

Contents

Purpose

This Procedure describes how clinical trials involving the University, whether as sponsor, a participating site, or in other capacities are conducted including trial development and approvals; reporting and monitoring during the trial; and site and trial close out.

Applicable governance instruments

Instrument	Section	Principles
National Statement on Ethical Conduct in Human Research	All	N/A
International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use. Guideline for Good Clinical Practice E6(R2) (ICH-GCP)	All	N/A
Safety monitoring and reporting in clinical trials involving therapeutic goods (NHMRC 2016)	All	N/A
ISO 14155:2020 Clinical investigation of medical devices for human subjects – Good Clinical Practice	All	N/A
Therapeutic Goods Act 1989	Section 18, 19, 31, 32, 41	N/A
Therapeutic Goods Regulations 1990	Regulation 12 Schedule 5A, 9, 9A	N/A
Therapeutic Goods (Medical Devices) Regulations 2002	Regulation 7.1, 7.3-7.5 Schedule 4, 5	N/A

Research Policy	Section 2: Responsible conduct of research Section 3: Research funding and costing Section 4: Research data and output	2.2 3.1 4.1, 4.2

Procedure

1. Background

The World Health Organization (WHO) has defined a clinical trial as: "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." An intervention may include experimental drugs, medical devices, health service changes, psychotherapeutic and behavioural therapies, treatments, or tests. In addition to the *National Statement on Ethical Conduct of Human Research,* and the *International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use Guideline for Good Clinical Practice* (ICH-GCP), trials that involve therapeutic goods are regulated by the Therapeutic Goods Association (TGA). This procedure is aligned with the requirements of these regulations, as well as University policies and procedures.

For guidance on whether your project would be classified as a clinical trial and other matters related to trial design and conduct visit the Clinical Trial Governance page.

The objectives of this procedure are to ensure that:

a) clinical trials conducted by the University and involving University investigators meet the legislative and professional standards of conduct and quality
b) University investigators and their Academic Unit understand the requirements for clinical trials and know how to seek specific advice
c) there is a standardised clinical trials approach across the University.

2. University involvement in clinical trials

The University may participate in a clinical trial as the trial sponsor, a trial site, or both, or in another capacity as per section 2.5.

Trial Sponsorship

2.1. All clinical trials must have an Australian entity which acts as a sponsor, which may be the University or other commercial or non-commercial entities.

2.2. If acting as sponsor, the University takes overall responsibility for the trial, including the initiation, management and/or financing of the trial. Unless otherwise approved by the DVC-R, the University may act as the sponsor when:

a) The research has been initiated by a University staff member or adjunct or clinical title holder.

b) The protocol has been developed by the University staff member or adjunct or clinical title holder.

c) The University will own any resulting intellectual property.

d) The benefits to the University and community outweigh the risks (including legal, financial, and reputational).

e) The University will be able to discharge its responsibilities as sponsor, including adequately monitoring the trial.

2.3. When a University investigator initiates a trial, the investigator has specific sponsorship responsibilities, including the development of the protocol and the management of the trial. These responsibilities are detailed below in sections 3 to 6.

Trial sites

2.4. All clinical trials take place at one or more sites, which may be at the University or other research institutions, in the public or private health sector, or in other settings.

a) A site is where participants are recruited and/or receive the intervention.

b) Each site must have a principal investigator (PI) who oversees trial conduct at that site.

c) The site may be a facility, location, or institution (or group of institutions) that resource, conduct and manage the clinical trial that come under one final research governance sign off (e.g. the University or another institution, such as the Tasmanian Health Service).

Other involvement

2.5. The University can be involved a clinical trial, other than as sponsor or site, including in the following capacities:

a) as an academic service provider (such as an advisor, contributor to development of the protocol)

b) as a clinical service provider (such as by providing tests or analysis to verify trial results or support clinical assessment)

c) as the supplier of the investigational product or device, or a placebo.

3. Trial development

Training and Qualifications

3.1. Clinical trials must be conducted by investigator teams that are sufficiently and appropriately trained and qualified as follows:

a) All University investigators, trial coordinators, project officers and any personnel who will be in direct contact with participants, must have current Good Clinical Practice (GCP) and University MyLO Clinical Trials training prior to participating in a clinical trial, which is to be kept current during the trial.

b) The investigator team must be made up of members that have the specific skills and training to complete the trial (such as relevant clinical expertise). The skills and training required will depend on the trial design. Curriculum Vitaes (CVs) showing relevant staff skills, experience and training, as well as relevant registration certificate(s) for health practitioners involved in the trial, are to be kept as part of trial documentation.

c) Any investigators external to the University with significant trial duties (such as an external site PI, or where involved in recruitment of participants, administering the trial intervention, or in safety monitoring) must also maintain GCP training, with certificates of completion kept as part of trial documentation.

3.2. The University PI is responsible for selecting investigators for the investigator team, and/or PIs for external sites, and ensuring that those investigators have the required training, experience, and qualifications.

3.3. The University PI must maintain a list of the qualifications of investigators who are responsible for significant trial-related duties at the site.

Trial Protocol, Risk Assessment and HoAU preliminary review

3.4. Creating the protocol is a sponsor responsibility. Where the University is the sponsor, the investigator team must prepare a trial protocol describing how the clinical trial will be conducted, guided by the SPIRIT checklist, and include the following:

a) Details of the scientific justification for the intervention and all proposed trial methods.

b) Plans for maintaining University PI oversight of trial conduct and participant safety at all sites. This should include a steering committee with a member who has relevant clinical expertise nominated to assess adverse events.

c) Scope and procedures for independent safety oversight of trials involving unapproved therapeutic goods or otherwise determined to be higher risk, such as an independent safety monitor, Clinical Event Committee, or a Data Safety Monitoring Board (DSMB). For further guidance see the NHMRC's *Safety monitoring and reporting in clinical trials involving therapeutic goods*).

d) Details of possible adverse events that may be expected during the trial, and plans for collecting, assessing, and managing adverse events that may occur.

e) Reporting protocols between sites, the University PI, the RGO and any relevant HRECs. This includes the preparation and submission of Annual Safety Reports to the reviewing HREC. This may form part of a separate document.

f) Triggers for when additional reporting to the University's Research Ethics Unit (REU) (and external HRECs as applicable), the RGO and the TGA (via the College of Health and Medicine (CHM)) or Research Hub is required (see section 5). This may form part of a separate document.

g) Plans for managing and storing trial data in accordance with the University's Data Classification Framework and the *Research Data Management Procedure*, with particular attention to the confidentiality of participant health information.

h) If applicable, plans for labelling and storing therapeutic goods in accordance with TGA guidelines, the Guide to Good Manufacturing Practice for Medicinal Products Part II, and any relevant import permits.

i) Other documentation required for ethical approval, including a Participant Information and Consent Form, a Case Report Form, and an Investigator Brochure (if using therapeutic goods).

3.5. Where the University is sponsor, site or involved in the clinical trial in another capacity (see section 2.5) the PI must prepare a risk assessment based on the protocol and the nature of the University's involvement outlining the trial risks and mitigation plans, for example:

a) risks due to the intervention, such as anticipated adverse events or supply of the intervention

b) risks due to the trial design, such as maintaining staffing and supplies at multiple sites

c) risks due to contributing to a clinical trial where the University is not site or sponsor such as providing analytical services or data analysis that could impact patient care

Guidance for development of clinical trials risk assessments.

3.6. The PI is responsible for preparing the trial protocol (when sponsor) and risk assessment (for all involvement types).

3.7. Where a University PI is also acting as a site PI for another institute or organisation involved in the trial, a Conflict of Interest Management Plan is required to be developed by the PI and the Head of Academic Unit (HoAU).

3.8. The HoAU, or their delegate, must review and approve the trial protocol and risk assessment (section 3.4 -3.5), and Conflict of Interest Management plan where appropriate, prior to submission for University clinical trial governance authorisation (see section 4) and confirming that:

a) the project aligns with the University's strategic direction, the academic unit research priorities and has academic merit

b) they have reviewed the risk assessment and the risks posed by the trial have been adequately

identified, will be appropriately mitigated, and are within the institution's risk appetite

c) the investigator team has the appropriate skills and training for the proposed trial

d) any academic unit facilities and equipment are suitable and available for the length of the proposed trial

e) the trial budget adequately covers the estimated costs of the trial (including any additional insurances that may be required), as per the *Research Funding Costing Procedure*.

3.9. University investigators are strongly encouraged to contact the RGO early in the trial development process for advice and to prevent delays in the governance authorisation process. Additionally, they should engage with their HoAU and other clinical trial investigator teams for guidance on local practices.

4. Trial approvals

Collaborations

4.1. Collaborative research must be carried out in accordance with the *Collaborative Research Procedure* including appropriate due diligence must be conducted for collaborations, and arrangements with foreign entities must be assessed for legal compliance and the risk of foreign interference.

Ethics

4.2. The requirement for ethical approval must be determined by review of the *Research Ethics Procedure*.

a) Ethics approval must be obtained from the University's HREC if the University is acting as either site or sponsor.

a) Ethics approval may not be required the University is involved in the clinical trial in another capacity.

4.3. Applications to the University's HREC must be in accordance with the *Research Ethics Procedure*.

4.4. If the project is sponsored by the University and is to be undertaken outside of Tasmania, the University PI must also:

a) obtain approval from an NHMRC registered ethics committee(s) in the relevant state(s); or

b) obtain approval from the overseas ethics committee(s).

Insurance

4.5. All clinical trials, regardless of the type of involvement (site, sponsor and other) must be entered on the University's clinical trial insurance register.

4.6. Clinical trials are covered by a separate policy and it is the PIs responsibility to ensure the trial is suitably insured by engagement with the University Insurance team. Additional insurance may be required if the trial includes the following, and must be budgeted for in the project:

a) neonates;

b) pregnant women, breast feeding women and infants breast fed by the trial participants;

c) international sites;

d) COVID-19 prevention or treatment.

4.7. Once suitable insurance has been sourced, the trial will be entered onto the insurance register. For site and sponsor involvements this is completed by the CHM Hub as part of the Governance Application Form (section 4.11) and for other involvement this is completed by the Research Governance Office.

Other Involvement

4.8. For clinical trials where the University is involved, but not as site or sponsor, full clinical trial governance authorisation is not required, however the following must occur:

a) A risk assessment to be completed by the PI which assesses the risk related to the activities the University will be undertaking in the trial

b) Approval of the risk assessment by the appropriate delegate with the necessary residual risk acceptance delegations under the *General Delegations Ordinance*

c) Ethics approvals, contracts and insurance as required

d) Approval by the appropriate research delegate in accordance with the *General Delegations Ordinance*

Site and Sponsor - Clinical trial governance authorisation

4.9. All clinical trials involving the University as site or sponsor must be authorised by the Deputy Vice-Chancellor Research prior to commencing (clinical trial governance authorisation).

4.10. The University PI is responsible for applying for clinical trial governance authorisation by submitting the Governance Application Form (GAF) to the CHM Research Hub. The CHM Research Hub will facilitate trial authorisation through the GAF and ensure that the PI has liaised with the relevant teams (Post-Award Research Funding team, legal services, insurance and the RGO).

4.11. The GAF includes the following information:

a) details of the investigator team, their roles and training

b) site contact details

c) budget

d) risk assessment

e) HoAU preliminary review and approval

f) any required contracts (such as Clinical Trial Research Agreements and subcontracts to third parties) have been executed by the appropriate delegate in accordance with the *Management of Research Funding Procedure* and the *General Delegations Ordinance*

g) proof Post-Award Research Funding team has facilitated review of contract risks by the legal team

h) confirmation that a Sponsor Audit Plan (as per 4.12) has been developed by the RGO for University sponsored trials

i) ethics approvals and insurance as required.

4.12. For University sponsored trials, the RGO will prepare a Sponsor Audit Plan, detailing the scope and frequency of auditing required to manage the risks outlined in the risk assessment and ensure that risk mitigation measures are effective. The scope and frequency of auditing required will depend on the trial design. Standard items to be audited include:

a) tasks are delegated to staff with appropriate to skills, experience, and training

b) consent from participants is obtained in accordance with current ethically approved documents

c) safety events are being recorded and assessed according to the approved protocol, with participant safety at the forefront of all decisions to amend or deviate from the protocol

d) records of shipping, dispensation, returns and destruction of therapeutic goods (if applicable).

4.13. Where the University is the sponsor, the University PI must also register the trial on a World Health Organization-listed trial registry before clinical trial governance authorisation will be granted.

4.14. Where the University is sponsor and the trial is being conducted at non-University sites (such as

Tasmanian Department of Health sites), the University PI must also obtain relevant site-specific approvals (e.g., governance approval) from those sites prior to commencing the trial.

4.15. For University sponsored trials involving unapproved therapeutic goods, once clinical trial governance authorisation has been obtained, the CHM Research Hub will submit a Clinical Trial Notification (CTN) application to the TGA. The University PI must arrange for payment of the TGA fees for CTN before starting trial recruitment.

4.16. If the UTAS sponsored trial involves high-risk or novel treatments (where there is no or limited knowledge of safety) the University HREC may direct that the trial be regulated under the Clinical Trial Approval Scheme (CTA), also run by the TGA. Additional consideration will be required for CTA trials; in these cases, the PI must contact the RGO to assist with CTA applications.

4.17. Once the GAF is complete, the PI and the HoAU will sign the completed GAF and the CHM Research Hub will create a record for the trial in the University's Clinical Trial Database and seek clinical trial governance authorisation from the DVC-R.

5. Trial conduct, reporting and monitoring

5.1. It is a shared responsibility of the PI, the investigator team at each site and the sponsor overall to ensure that the ethically approved trial protocol is followed appropriately.

5.2. Investigators must also ensure the data management plan outlined in the trial protocol is followed, including the specified timeframes for the retention of data.

5.3. Where the University is the sponsor, the University PI must keep the trial registration current throughout the trial.

Reporting

5.4. Where the University is sponsor or site, the University PI must ensure that routine progress reports are submitted to the University's HREC in accordance with the ethics approval (normally annually).

5.5. If the University is the sponsor, the University PI must develop an Annual Safety Report, reviewed by the trial oversight structures (see sections 3.4 b and c) which includes a clear summary of the evolving safety profile of the trial. This is to be submitted to the University HREC and any other relevant HRECs.

5.6. For University sponsored trials, the University PI is responsible for ensuring that progress reports are also submitted in accordance with any contractual obligations (for example milestone reports to funders).

5.7. A summary of current activity and monitoring outcomes for each academic unit will be provided from the RGO periodically to the HoAU.

Amendments to the protocol

5.8. For clinical trials involving the University as sponsor or site, any amendments to the protocol, such as changes to trial sites, procedures or investigators must be approved by the University's HREC before being implemented.

5.9. The protocol may need to be deviated from when a measure is required to be taken to eliminate an immediate hazard to a participant's health or safety. This can be instigated by either the investigator or sponsor and implemented before seeking approval from the HREC or University by following the process set out in the NHMRC's *Safety monitoring and reporting in clinical trials involving therapeutic goods*.

5.10. The RGO will also consider the impact of the amendments on any contractual arrangements for the trial. If contract variations are required, these will be managed according to the *Management of Research Funding Procedure*, and notification made to the RGO by the Post-Award Research Funding team.

5.11. If the amendment will result in material changes to University workloads, budgets or facility use, or

other items in section 3.8, the PI should discuss these with their HoAU to ensure the continued feasibility of the project and revise the risk assessment accordingly.

5.12. If the trial required ethics and/or governance approval from an external committee or body (for example where the trial is being conducted at a non-University site), prior approval of that external committee or body must also be obtained by the University PI before the amendment is implemented.

5.13. For University sponsored trials registered with the TGA, the University PI must advise the CHM Research Hub if there are amendments to the registered information. The CHM Research Hub will then coordinate approval of the amendment by the TGA. An additional fee may be charged by the TGA, which is payable by the PI from the trial budget.

Monitoring

5.14. During the trial, conduct is to be reviewed by:

a) the internal review processes set up in the Protocol (section 3.4)

b) the Research Ethics Unit (REU), through review of progress reports, safety reports, amendments, and protocol deviations (sections 5.4, 5.5, 5.8)

c) RGO monitoring of submissions to the REU (section 5.14 b) and auditing as per the Sponsor Audit Plan (sections 4.12 and 5.15)

d) additional monitoring may also be conducted by external sponsors or organisations such as the TGA (for CTN or CTA trials).

5.15. For all trials, the RGO will review submissions to the REU such as progress reports, safety reports, amendments, and protocol deviations to check for items that may trigger additional governance review.

5.16. For University sponsored trials, the RGO will audit trial conduct in accordance with the agreed Sponsor Audit Plan (see section 4.12). RGO may also conduct additional investigations if triggered by requests from HREC, colleagues, participants, or the outcome of routine monitoring.

5.17. Outcomes from RGO monitoring will be reported to the University PI. Other parties such as the University HREC, DVCR and TGA may also be notified by the RGO when required.

5.18. If a suspected integrity breach is identified during monitoring, this will be reported in accordance with the *Research Integrity Complaints Procedure*.

5.19. If monitoring reveals sufficient concern for trial conduct, for example a series of serious breaches of the approved protocol, the RGO or HREC may recommend that the DVCR suspend or revoke clinical trial governance authorisation.

Safety issues and protocol deviations

5.20. In the event of a safety issue or a protocol deviation, the University PI must notify the University REU and the CHM Research Hub in line with the trial protocol and guidance on the Human Research Ethics website. The PI should also notify the HoAU of significant safety issues and reassess relevant risk mitigation strategies.

5.21. For externally sponsored trials, if the significant safety issue, or protocol deviation occurs at a University site, it is the responsibility of the University PI to advise the trial sponsor immediately.

5.22. For University sponsored trials where the clinical trial involves a CTN or CTA, the CHM Research Hub must advise the TGA of safety events (section 5.20) within the required timeframes.

6. Trial completion, termination, or suspension

6.1. When the University is sponsor, once recruitment, treatment and follow-up are completed and no further data are to be entered into the source database for that site (site closeout), the University PI is responsible for ensuring the following for any University sites and coordinating with any external site PIs for all external sites:

a) equipment or supplies (including investigational products) are returned or destroyed in accordance with site agreements

b) biological samples are stored, analysed, or destroyed in accordance with the trial protocol

c) all documents and data are managed in accordance with the data management plan

d) any site specific close out requirements, such as notification to approval HREC through final reporting and/or governance offices

e) any financial reconciliation required between site and funder has been completed

f) notifying the CHM Research Hub and any University facility managers for University sites.

6.2. For externally sponsored clinical trials involving University sites, following site closeout the University PI is responsible for:

a) notifying the CHM Research Hub and any University facility managers

b) working with the sponsor to ensure that all items in 6.1 are completed in a timely manner.

6.3. When all analyses have been completed for the trial (trial closeout), University PI must advise the RGO and submit the final report to University HREC, and any other agencies involved in the trial such as funders or external HRECs.

6.4. If a trial is terminated or suspended by an external sponsor, the University PI is responsible for ensuring the University HREC and RGO have been notified.

6.5. After trial closeout, the University PI is responsible for ensuring that physical and electronic copies of Trial and/or Site Master Files, including source materials and data are appropriately archived as per the *Information Management Procedure*, data management plan and the ethically approved protocol as follows:

a) any applicable destruction dates required by ethical approval must be clearly indicated

b) any biological specimens to be kept in long term storage must also be clearly labelled with contact information and destruction dates noted.

6.6. When notified that the trial closeout has occurred, the CHM Research Hub (site and sponsor involvement) or RG (other involvement) will update the insurance register.

Related procedures

Research Ethics Procedure

Research Data Management Procedure

Research Funding Costing Procedure

Management of Research Funding Procedure

Information Management Procedure

Versions

Version	Action	Approved by	Business Owner/s	Approval Date
1	Approved	Deputy Vice-Chancellor (Research)	Executive Director, Research Operations	3 November 2022
2	Approved	Deputy Vice-Chancellor (Research)	Executive Director, Research Operations	25 October 2023
3	Approved	Deputy Vice-Chancellor (Research)	Executive Director, Research Operations	16 October 2024